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1. A. W. Spittler, Col., (M.C.), U.S.A., J. J. Brennan, Lt. Col., (M.C.), U.S.A., J. W. Payne, Capt., U.S.A.F. (M.C.), American Academy of Orthopedic Surgeons, Jan. 26-31, 1952, Chicago, Illinois.
2. M. C. Cobey, M.D., F.A.C.S., Professor of Orthopedic Surgery, Georgetown University and Senior Attending Orthopedic Surgeon, Children's Hospital, Washington, D.C., The American Surgeon, Vol. XVIII, No. 4, April, 1952, pp. 413, 415.
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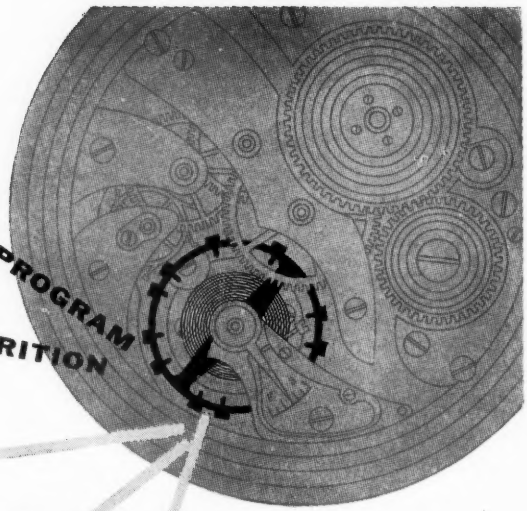

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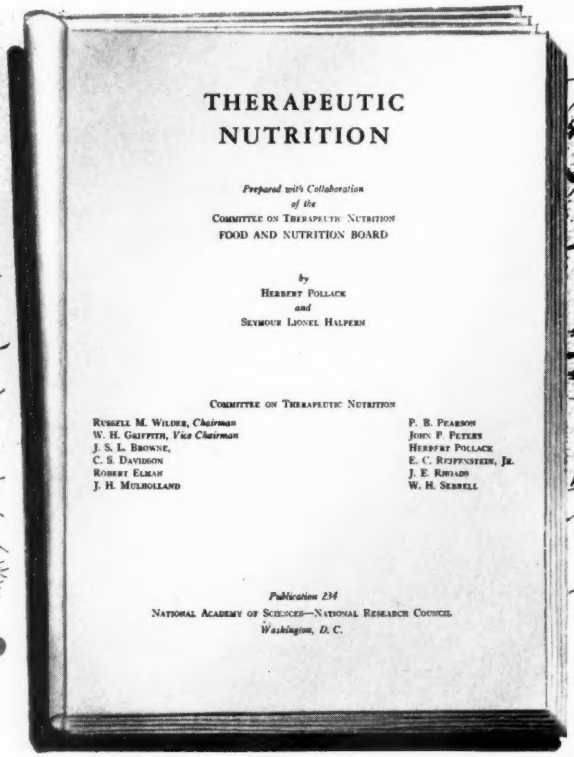

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SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 98 JANUARY, 1954 NUMBER 1

ESOPHAGEAL DIVERTICULA

FRANK H. LAHEY, M.D., F.A.C.S., and KENNETH W. WARREN, M.D., F.A.C.S.,
Boston, Massachusetts

WE HAVE attempted in this article to summarize and to bring up to date our observations on the two stage operation for pharyngoesophageal diverticula. We have in previous articles (13–30) reviewed the literature on this subject and some of these historical data which we published (13, 24) in 1923 and 1940 are included in this article in order that our current comments concerning the various aspects of the development of our knowledge of these lesions may be held in proper perspective.

We shall present our experiences with operations upon 365 patients (to May 15, 1953) with pharyngoesophageal pulsion diverticula and operations upon 9 patients with epiphrenic pulsion diverticula. A great many traction diverticula are seen here in the course of routine examinations of the esophagus, and their management, largely conservative, will be discussed in the text of the paper.

Consideration is given in this discussion to the physiology of swallowing in relation to the development of pharyngoesophageal diverticula. The origin and complications of traction and epiphrenic esophageal diverticula are likewise considered.

A follow-up study, including complications and recurrences, in 250 pharyngoesophageal diverticula is included in this discussion. This figure of the first 250 cases followed was selected in order to review a series of cases in which operation had been done early enough to permit time to have elapsed during which recurrences could have taken place. If there has not been a recurrence, there have been no other late complications.

HISTORICAL DATA

In 1764 Ludlow observed "preternatural pockets" in the esophagus at autopsy. It is interesting in comparing it with our present knowledge to note how accurate the description of this condition is in this article published in 1767. In 1816 Sir Charles Bell published in his volume of *Surgical Observations* a paper entitled "A Praeternatural Bag, Formed by the Membrane of the Pharynx."

CLASSIFICATION

In 1877, Zenker and Ziemssen were the first to classify diverticula of the esophagus into traction and pulsion types. They illustrated a point then unrecognized which we have stressed in our descriptions of this lesion when it causes obstruction, that is, the fact that the opening into the large pharyngoesophageal diverticulum is directly downward and the

Dr. Lahey began his correspondence with the Editor in May 1953 concerning this manuscript which describes the entire experience at the Lahey Clinic with esophageal diverticula. It represents, perhaps, the largest experience of a single individual at least with pharyngoesophageal diverticula, traction diverticula, and epiphrenic diverticula. The postscript written in his own handwriting read "P.S. There is so much debate about the one stage and the two stage operations that I wanted to present all of our views on the two stage operation." Dr. Lahey's death occurred June 27. 1953.—EDITOR.

opening into the esophagus is lateral, making the entry of food or an esophagoscope into this lateral orifice difficult. This, in our description of pharyngoesophageal diverticula, would represent the third stage, the obstructive stage, as shown diagrammatically in Figure 4a.

In 1922, Bensaude, Grégoire, and Guénaux made a new classification of esophageal diverticula in which those of the esophagus per se were distinguished from pharyngoesophageal diverticula. In their article, in which the first adequate classification of the types of diverticula is given, is shown an epiphrenic diverticulum of the esophagus immediately above the diaphragm, which is typical of the diverticulum we see today.

In 1840 Rokitansky first correctly described traction diverticula.

THE PHYSIOLOGY OF SWALLOWING AND ITS RELATION TO PHARYNGOESOPHAGEAL DIVERTICULUM

Since the act of swallowing plays such an important part in the production of a pharyngoesophageal diverticulum, a simple explanation of this mechanism should be outlined in any discussion of this subject. For those more deeply interested in the mechanism of swallowing, no more comprehensive description exists in the literature than that of Negus, published in the October 1950 issue of the *British Journal of Surgery*. This extremely complete article discusses the anatomy, the muscles involved, their innervation and the co-ordinated mechanism in the human being of the process of propelling food from the mouth to the pharynx and into the esophagus. A further discussion of the act of swallowing described from the point of view of the endoscopist is available in the book on esophagology by Jackson and Jackson. This latter description of the mechanism of swallowing is valuable since it is presented from a within-out view, that of the esophagoscopist, rather than from the without-inward view of the anatomist or operating surgeon. Further description of this process by which food intake is accomplished and propelled into the stomach is given in Best and Taylor's book, *Physiological Basis of Medical Practice*.

As this article is primarily concerned with the clinical aspect of esophageal diverticula and their surgical management, it seems best to refer only to these articles and to discuss the process of swallowing in the simplest possible terms so that its relationship to the production and progress of a pharyngoesophageal diverticulum can readily be comprehended.

If one will consciously swallow and attempt to make oneself actively aware of what happens by holding on to the larynx, the voluntary portion of this physiologic process can be clearly appreciated. As stated by Negus, the longitudinal fibers of the muscular pharynx, consisting of the palatopharyngeus, palatolaryngeus, stylopharyngeus, salpingopharyngeus, the tensor veli palatini and levator veli palatini, function as a group to elevate the whole pharynx at the beginning of the second stage of swallowing. This can readily be appreciated when one feels of the pharynx as swallowing is initiated and one can demonstrate the prompt rise of this structure toward the hyoid which is, in turn, drawn up toward the mandible. Thus the pharynx is pulled up over the bolus of food which is prevented from upward movement by the sphincter-like action of the tongue, fauces, and the nasopharyngeal sphincter. This is the first stage of swallowing. As one consciously swallows, both of these segments of the act are plainly and easily recognizable. The nasopharyngeal sphincter is readily perceived as being closed by the observer on himself (the first stage). The pharynx can next be felt to rise over the bolus of food and against this closed nasopharyngeal sphincter. As this portion of the swallowing act is accomplished (second stage), a peristaltic wave is initiated by the pharyngeal constrictors, beginning in the nasopharynx, passing downward and ending at the pharyngoesophageal junction (third stage.)

It is here that the act of swallowing is related to the production of a pharyngoesophageal diverticulum. It is to be noted in Figure 1 that the lowest inferior constrictors and the cricopharyngeal fibers are given off obliquely at the pharyngoesophageal junction and produce in this small triangular area a weak spot at the pharyngoesophageal junction

which has frequently been spoken of as the pharyngeal dimple, previously discussed by us and many others in writing on this subject.

With the establishment of a peristaltic wave in the pharyngeal constrictors there must at this moment occur a co-ordinated relaxation of the cricopharyngeal sphincter to permit the unobstructed propulsion by the constrictors of the mass of food into the esophagus (fourth stage). It is when inco-ordination in the process of swallowing occurs at this point of sphincter-like constriction of the cricopharyngei at the pharyngoesophageal junction that undue pressure is made upon this posterior weak point at the junction of the constrictors with the diverging fibers of the cricopharyngei, the pharyngeal dimple, and it is at this point, as with an inguinal hernia, that a false diverticulum occurs. This is brought about by the mucosa and submucosa bulging through this dimple, lightly covered, as it is, by the weak fibers of the cricopharyngei. The lowest fibers of the inferior constrictor bulge out with the weak cricopharyngeus fibers over the dimple to form the first stage of a pharyngoesophageal diverticulum, as shown in Figure 1.

A very practical description of the esophagus and its weak points is presented by Jackson and Jackson. The sphincteric action of the cricopharyngei, as well as the cardia, is diagrammatically illustrated in this article by a rubber tube with a clamp or pinchcock (Jackson) at the upper end representing the sphincteric action at the pharyngoesophageal junction by the cricopharyngei muscle, and a clamp or pinchcock at the lower end representing the sphincteric action at the cardia. It is this improperly co-ordinated sphincter-like action of the cricopharyngei that interferes with the normal, co-ordinated relaxation of the sphincter to permit it to open properly and accept the bolus of food which, as previously stated, causes the pressure at the weak point in the pharyngoesophageal junction, the pharyngeal dimple, which causes the bulge here, and because of this Chevalier Jackson was prompted to speak of the action of this sphincter as the "pinchcock effect."

With the establishment of a bulge at the junction of the pharynx and the esophagus,

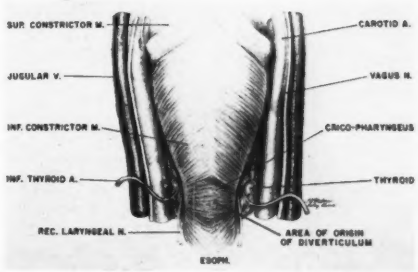


Fig. 1. Diagrammatic illustration of the anatomy on the posterior wall of the pharyngoesophageal junction. Note the lowest fibers of the inferior constrictor and the oblique fibers of the cricopharyngei, and the area of origin of the false pharyngoesophageal diverticulum through these fibers.

the eventual production of a pharyngoesophageal pulsion diverticulum is merely a matter of frequent repetition of obstruction here during the descent of the bolus of food until the sac made up of mucosa and submucosa of the pharynx attains sufficient size to hold food and mucus. It is then capable, by the weight of its contents and by repeated distentions, of attaining greater and greater proportions until it acquires all of the characteristics of a pharyngoesophageal diverticulum, as shown in Figures 2, 3, and 4. At this point of development there is an aperture at the neck of the sac, at the pharyngoesophageal junction connecting the diverticulum with the esophagus, varying in diameter and in length in different individuals in relation to the period of time the sac has existed. Finally, a sac is developed varying in diameter, in length, and lowness of level in the mediastinum to which it has descended, again depending upon how long it has existed and how much and how frequently it has been distended by increased pharyngeal pressure.

The mechanism of the production of a pulsion pharyngoesophageal diverticulum, as described, is not a complicated one. As it increases in size, the sac itself increases in length, and since its origin must always remain a fixed point, at the level of the cricoid at the pharyngoesophageal junction, its transverse diameter, while it is still in the neck, must always remain relatively limited by the muscular structures of the neck surrounding

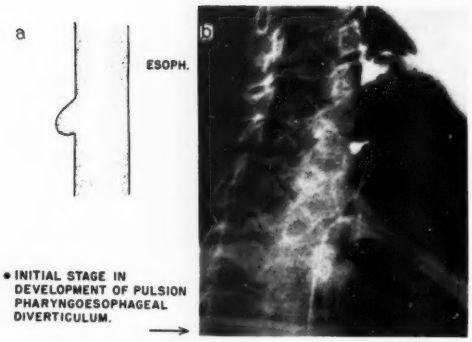


Fig. 2. In these two illustrations, one diagrammatic (a) and the other a roentgenogram (b), is shown the first stage development of the pharyngoesophageal diverticulum. This is the stage of bulge without the true development of a good sac.

it. Its direction of enlargement, therefore, must be chiefly the only unobstructed pathway along which it can enlarge, that is, downward and into the mediastinum. It is for this reason that the small pharyngoesophageal diverticula remain largely globular in character, but become elongated as they descend downward into the mediastinum and again often become globular as they reach the mediastinum where lateral expansion is unrestricted.

The downward descent of a pulsion pharyngoesophageal diverticulum, once the sac has attained any considerable size, has to do with the weight of its food-filled sac, through its dragging action, and the ascent and descent during swallowing of the food, not unlike the action that guides an adenoma of the thyroid, which has become intrathoracic, into the superior mediastinum.

In discussing this phase of the enlargement of an esophageal diverticulum in past articles, one of us (F.H.L.) has particularly stressed the point that this stage of the descent of the diverticulum plays a very important part in the kind of symptoms which are associated with the different stages of the development of a pharyngoesophageal diverticulum.

We have arbitrarily divided the different stages of development of a pharyngoesophageal diverticulum into three phases. (1) The first phase is shown diagrammatically in Figure 2a, in which no sac exists but only the first bulge of mucosa and submucosa through the triangular weak point at the pharyngoesophageal junction, spoken of here as a pharyngeal dimple. It is obvious that no symptoms can occur other than the temporary retention of food of such character that it can adhere to the alcove-like bulging mucosa. It is at this stage, as one of us (F.H.L.) has previously described, that the only symptoms are those of a feeling of lodging of a foreign body at this bulging point, producing attempts to dislodge it by hawking. It is obviously impossible and improper to attempt to deal surgically with an esophageal diverticulum at this stage of its development. One should await the further development of the diverticulum until there is a definite sac with a definite neck, which will lend itself to its surgical demonstration and resection and to safe and adequate ligation or suture of the neck of the sac flush with the esophagus so that no portion of the sac remains to promote a recurrence. That this is not always the process of development is shown by Figure 2b in which is demonstrated a fully formed diverticulum of minute proportions with a definite neck and sac. It is obvious from this illustration that in certain cases very small but perfectly formed sacs can develop as a first stage in this condition. One should in the presence of these perfectly formed small sacs likewise wait for develop-

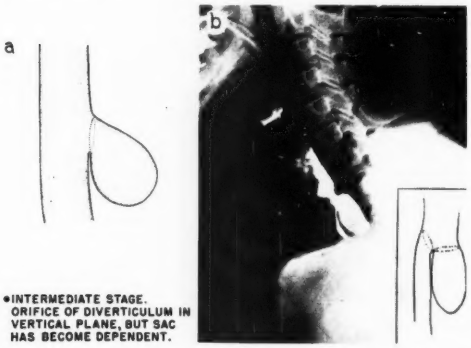


Fig. 3. In a is shown diagrammatically the second stage of the development of a pharyngoesophageal diverticulum. Note that the opening into the diverticulum is still on the lateral wall of the esophagus, while in b is shown the gradual conversion from the second stage of the development of the diverticulum to the third stage. Inset, Diagrammatic illustration of the third stage.

ment of the sac to such a size as to make it easy to find and dissect the neck and main portion of the sac to insure safe removal at the second stage operation.

In the presence of undue muscular weakness at the pharyngeal dimple and the abnormal intrapharyngeal pressure resulting from failure of the cricopharyngeal sphincter to open during the act of swallowing, pressure continues and the second stage of a pharyngoesophageal diverticulum is developed, as shown in Figure 3a and b. One of us (F.H.L.) has stressed in all articles on this subject that the sac is now globular in shape, that the opening of the diverticulum into the esophagus itself is still laterally placed on the esophageal wall (Fig. 3a) and that although some food will enter the diverticulum (Fig. 3b), there will still be a direct pathway into the esophagus into which much of the bolus of food is directly propelled on its way to the stomach. It is in this stage that the symptoms related to this type of pharyngoesophageal diverticulum are solely those that are the result of the accumulation of food, fluid, and mucus within the globular sac of the diverticulum and are unassociated with any degree of esophageal obstruction. These symptoms consist of the occasional regurgitation of food taken at a previous meal, regurgitated at any unpredictable time, during the swallowing of another meal, between meals, or with turning of the head from one side to the other. They result from the pressure of the omohyoid, the sternocleidomastoid and the prethyroid muscles on the filled or partially filled sac. This regurgitation can occur in the middle of the night as the patient turns from side to side, and occasionally results in awakening the patient as the ejected food is inhaled into the larynx. These symptoms of the second stage of an esophageal diverticulum caused by aspiration of fluids and food regurgitated from the diverticulum have brought a number of patients to us for surgery because it is so frightening to them to be awakened by the resulting choking from aspirated food, because it has interfered with sleeping or because in a few instances such aspiration of food has resulted in lung infections as well as lung abscesses.

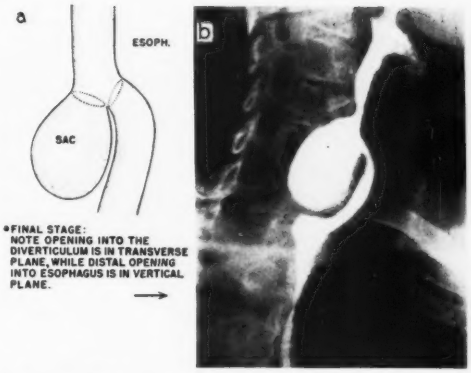

a
ESOPH.
SAC
*FINAL STAGE:
NOTE OPENING INTO THE DIVERTICULUM IS IN TRANSVERSE PLANE, WHILE DISTAL OPENING INTO ESOPHAGUS IS IN VERTICAL PLANE.
b

Fig. 4. Third stage of the development of a pharyngoesophageal diverticulum. In a, note the diagrammatic illustration of the change of the opening into the diverticulum into a completely transverse one and the change of the opening into the esophagus itself into an oblique one. This is well shown in b. Note again the diagnostic demonstration that this is a true pharyngoesophageal diverticulum identified by the spill-over at the top of the sac, thus distinguishing it from a possible esophageal web. b, This roentgenogram also demonstrates how impossible it is to pass an esophagoscope or bougie through the lateral opening into the esophagus at this stage of the development of the diverticulum.

We are particularly anxious to discuss the third stage of pharyngoesophageal diverticula and their symptomatology, since one of us (F.H.L.) has, over the years, called attention to the explanation of the obstruction to the descent of food into the esophagus in this stage. As the result of this obstruction this stage is associated with severe degrees of inanition because the patient does not obtain an adequate amount of food.

In Figure 4a and b is shown the mechanism of the production of esophageal obstruction in the third stage of the development of a pharyngoesophageal diverticulum. In Figure 3b is shown a roentgenogram in which, even though the esophageal diverticulum is relatively small, the principle is well demonstrated as to why interference with swallowing occurs in these cases. In this illustration as well as in Figure 4 is shown how impossible it is in this third stage of a pharyngoesophageal diverticulum to pass an esophagoscope or bougie into the esophagus itself, since this stage converts the true opening into the esophagus into a lateral slit (Fig. 4), into which the rigid

esophagoscope or bougie cannot be manipulated. In Figure 5a is illustrated such a case in which an attempt was made elsewhere by an inexperienced resident to pass an esophagoscope, which resulted in perforation at the tip of the sac. In Figure 5b is illustrated the remaining sinus tract in the mediastinum after recovery from the mediastinitis.

The mechanism of the production of esophageal obstruction in the large elongated sacs (the third stage of esophageal diverticula) is based upon the fact that the large, food-filled pharyngoesophageal diverticulum is dragged farther and farther downward into the mediastinum until the pull of this food-filled and weighted sac converts the opening into the diverticulum itself from a lateral one (Fig. 3a) into a transverse one, and the lips of the opening into the esophagus itself are approximated on the lateral wall by the downward traction of the large food-filled intrathoracic pharyngoesophageal sac, making possible the passage of food into the esophagus only by spill-over from the diverticulum (Fig. 4b).

At this stage all the symptoms related to the second stage of a pharyngoesophageal diverticulum are still present. There are gurgling noises as the patient swallows, and regurgitation of food. At the third stage, however, are added the symptoms of varying degrees of obstruction dependent upon the size of the sac and how deeply it has progressed into the mediastinum. At the third stage of the development of a pharyngoesophageal diverticulum the peristaltic waves of the constrictors propel the food, not into the esophagus itself, but into the pharyngoesophageal diverticulum with its transverse opening. It is at this stage that the patients, because of the real obstruction, as shown in Figure 4b, reach advanced stages of emaciation and constitute serious operative problems because of the long period of time over which they have existed without adequate food intake, and the sac becomes larger and larger as it is distended with a greater and greater amount of food.

DIAGNOSIS

The diagnosis of pharyngoesophageal pulsion diverticula and the demonstration of the stage to which they have developed are almost entirely dependent upon their demonstration on roentgenograms after the patients have swallowed thin mixtures of barium. We have not found it necessary to employ esophagoscopy either as a diagnostic procedure or as a part of the operative procedure as these sacs are dissected free from their overlying anatomic structures, and believe that, except in the hands of those who are expert and experienced in esophagoscopy, in these particular cases it is dangerous.

There are one or two warnings that we would like to make concerning the diagnosis of these pharyngoesophageal diverticula before discussing their surgical management and the other two types of esophageal diverticula, traction and epiphrenic. A warning should be sounded that a roentgenologic diagnosis of pharnygoesophageal pulsion diverticulum should not be made solely on an anteroposterior roentgenogram following the ingestion of a thin barium mixture. When a barium-filled esophagus is seen solely from an anteroposterior viewpoint, as shown in Figure 6, an esophageal web can closely simulate the spherical globular type of esophageal dilatation which characterizes a second stage pharyngoesophageal diverticulum. We have made this mistake twice and have been much distressed by failure to find the sac on exploration. In both of these cases we demonstrated that the condition was due to a dilatation of the esophagus above an esophageal web. If a semilateral view of the diverticulum had been made in these cases, the absence of the characteristic spill-over from the top of the diverticulum into the esophagus itself would have saved us from this mistake. In such a semilateral view of the barium-filled diverticulum one must be able to demonstrate the thin stream of barium spilling over from the neck of the sac where it enters the esophagus itself. This distinguishes it as truly a pharyngoesophageal diverticulum and not as a dilatation of the esophagus above a web (Fig. 6). In such a dilatation, a trickle of barium into the esophagus sometimes can be seen emerging from the lowest point of the dilated esophagus above the web. As shown in Figure 4b this distinguishing spill-over point can readily be seen and is dependable evidence that the spill-

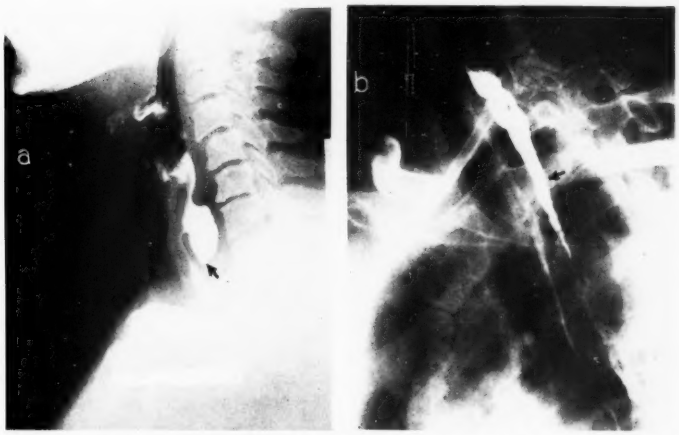


Fig. 5. a, In this illustration is shown the teat-like projection (arrow) at the end of the sac of the diverticulum which represents the point of perforation by the esophagoscope passed into the sac instead of into the esophagus itself. b, In this illustration is shown the barium filled mediastinal sinus tract, indicated by an arrow, after the patient had recovered from the mediastinitis.

over is at the top of the sac and not from the bottom, as with an esophageal web.

The need for this differentiating semilateral roentgenologic view of the spill-over from the top point is intensified by an experience with a patient who was recently sent to surgery with only an anteroposterior view of what appeared to be a pharyngoesophageal diverticulum (Fig. 6). This patient was put on the operating list for surgery by one of the members of the gastroenterologic service who was unfamiliar with the confusing similarity of a dilatation above a web and a true pharyngoesophageal diverticulum in a barium roentgenogram taken only in the anteroposterior position. The sac was found to be due to a web and was not a pharyngoesophageal diverticulum. This operation could have been avoided had a roentgenogram of the barium-filled esophagus been taken in the semilateral position.

Another point we wish particularly to call attention to in the roentgenologic diagnosis of such diverticula is the fact that any irregularity in the outline of the barium-filled sac must suggest the possible presence of a malignant lesion within the sac (Fig. 7). This occurs rarely, but when the diagnosis is suspected preoperatively, the surgeon should be prepared to deal more radically with such a lesion than would be the case in the removal of a benign diverticulum.

We wish to record another warning particularly concerning pharyngoesophageal diverticula of the pulsion type in the third stage, that is, that attempts to pass a bougie in such cases can result in perforation of the end of the sac and the production of mediastinitis. Five such cases have been sent to us following perforations elsewhere. We strongly urge esophagoscopists who are not experienced in dealing with sacs of this type not to insert bougies blindly, particularly in the second or third stage of the development of a pharyngoesophageal pulsion diverticulum. In bougienage of patients with a pharyngoesophageal diverticulum in stage two, or those patients who have previously had a diverticulum removed, we suggest that dilators be passed only on a previously swallowed string to insure proper guidance of the bougie into the esophagus itself. We urge further that should postoperative bougienage be undertaken, and in our experience it is rarely necessary, it should be realized that mucosal esophageal shelves can and occasionally do exist at the level at which the sac has been amputated and upon which bougies unguided by a swallowed string

can lodge, and that persistent pressure on the bougie can result in perforation of the tip of the diverticulum.

SURGICAL TREATMENT

In 1830, Bell proposed establishment of a fistula to empty the diverticulum of its contents; this was practiced in 1877 by Nicoladoni in Vienna, Austria.

In 1850, Kluge conceived the idea of excision, which was first done in 1884 by Niehans on a patient with both goiter and esophageal diverticulum.

In 1892, von Bergmann reported a case of successful extirpation, and in the same year Kocher performed the operation, with healing by first intention.

In 1896, Girard suggested a new method—invagination of the diverticulum and suturing of the esophageal walls. This method was revived in 1922 by Bensaude, Grégoire, and Guénaux.

In 1917, Bevan revived this procedure. He inverted the outer half of the sac and buried the stump with a series of purse string sutures. This operation never attained popularity because recurrences take place since the wall of the sac is so thin that adequate inversion stitches cannot be inserted. (Note: The operation did not include severing the cricopharyngei fibers below the neck of the sac, as discussed in our description of the modern operative procedure and, also, in a limited number of cases, the inverted sac was coughed up between the vocal cords and presented in the pharynx, requiring immediate action. Such an occurrence arose in the experience of Dr. Roy D. McClure and necessitated amputation, by the laryngologist, of the coughed up sac through the mouth with a snare, fortunately with complete recovery of the patient. Dr. McClure agreed that this was an undesirable method of treatment.)

In 1912, Schmid proposed diverticulopexy with the tip of the sac higher than the neck; this was performed on a patient in 1917 by Hill, with temporarily good results. Rarely do we perform the two stage procedure described in this article in which the apex of the sac, if it is not too large, is sutured between the first and second stages to the upper edge of the sternohyoid muscle, without a visitor asking, "Why do you not leave the sac fixed high in this position, parallel with the larynx, since food does not enter the sac between the first and second stages?" We have employed this plan in 4 cases, only to have the lower wall of the sac sag, again descend, and eventually require complete mobilization of the sac, ligation at its neck, and excision. It has been the experience of nearly everyone that diverticulopexy is followed by too many recurrences to make this a feasible and worthwhile procedure in this type of diverticulum.

From 1910 to 1915, the popularity of the surgical treatment of pharyngoesophageal diverticulum was inhibited by the high mortality associated with one stage procedures.

In 1909, Goldmann performed the first two stage operation; the pouch was freed, its pedicle ligated with silk, the wound packed, and the sac fixed to the surface of the wound. This procedure resulted in sloughing of the diverticulum, and on the eighth day a fistula formed, which healed in 2 months. We have never employed this procedure because it is unsound in principle, resulting as it does in slough, perforation, leakage, and contamination of the fascial planes and possibly the mediastinum.

In 1916, Murphy improved this method by implanting the diverticulum into the wound with its neck unligated, thus preventing sloughing, and resected it 2 weeks later. This was the first plan of two stage management of the pharyngoesophageal diverticulum which was sound in principle, surgically practicable, and followed by quite universally successful results.

In 1918, Judd reported a modification of this method; the edges of skin were sutured to the neck of the sac; the wound was closed, and the sac was left as in an unopened colostomy stoma, lying on the skin. Ten to 12 days later, when healing had taken place within the wound and about the neck of the sac, it was cut away and its edges were turned into the esophagus. This is an unnecessarily long interval as the sac is safely sealed into the wound in 7 days.

In 1933, one of us (20, 21) (F.H.L.) modified the two stage operation. In small sacs the tip

Fig. 6.

Fig. 7.

Fig. 6. This illustration demonstrates the dilatation above an esophageal web as seen anteroposteriorly which can be confused with a true pharyngoesophageal diverticulum. It is in such a case that the semilateral view will demonstrate by the spill-over at the top, as shown in Figure 4b, the true pharyngoesophageal diverticulum and not an esophageal web.

Fig. 7. Pharyngoesophageal diverticulum in which carcinoma occurred. As stated in the text, any irregularity in the outline of the sac should make one suspicious of the occurrence of carcinoma within the sac and the surgeon should be prepared to deal radically with such a situation.

of the sac after dissection was sutured to the sternohyoid muscle at a level higher than its neck within the wound, and in large diverticula the sac was implanted in the wound, pointing upward parallel to the pharynx. This prevented food from entering the wound between stages and caused the fistula which occurred after the second stage to close early. At this period of our experience the sac was not dissected as thoroughly as at the present time and the second stage consisted only of dissecting the mucous membrane out of the sac down to the opening into the esophagus, packing the resulting canal and allowing the tract to granulate in from the bottom. This plan was abandoned several years ago, and accurate ligation or suture of the neck of the sac substituted for it. In addition, the black silk stitches with which we now fix the tip of the sac to the sternohyoid edge can be used as a means of readily identifying the tip of the sac at the second stage removal.

Another type of procedure was the suggestion that the partition between the true esophagus and the sac parallel to it be severed through a laryngoscope, and this method was employed in 4 cases by Dr. Henry A. Mosher and his group at the Massachusetts Eye and Ear Infirmary. Obviously, the mortality in this unsound procedure was, as would be expected, excessive from mediastinitis and fascial plane infection, and it was promptly abandoned.

Before discussing the much debated problem of the one stage or the two stage operation in pharyngoesophageal diverticulum, we would like to state that the decision in the selection of the one or the two stage operation should be based upon the answers to two or three questions raised in the comparison of these two procedures. Outstandingly, the first question to be asked concerning both methods is the comparison of their mortality. The morbidity rates in both types of procedures must be compared; they are based on how many have leakage of the sac at the neck postoperatively, how long does this leakage of food and fluids persist, in how many cases are the sinuses either present for a long period of time or persist permanently, how many have required secondary operations to take care of the sinuses, in how many cases has mediastinitis occurred, in how many cases has empyema requiring drainage occurred, and in how many

cases has obstruction occurred from too radical amputation of the neck of the sac, requiring plastic procedures on the esophagus. Most importantly, one of the questions which must be asked concerning both methods is, what is the recurrence rate?

In any discussion of this subject, it must be stated that the comparative mortality rates by either method are low. In this series of 365 pulsion pharyngoesophageal diverticula there have been but 2 deaths, one in the first series of 20 cases, a man of 84 who died of uremia 4 days after the first stage of a two stage procedure, but whose death must be directly attributed to the operation, and a second death due to mediastinitis, fascial plane infection and empyema in a doctor 48 years of age, who was operated on over 10 years ago. The death was the direct result of an unrecognized perforation of the neck of the sac at the operation made during the course of the dissection on the opposite side (right) of the neck of the sac from the side upon which the incision was made and the dissection done. Had this perforation been discovered at the time of the first stage procedure, when it was done, we might very well have saved this patient's life. It is, in a considerable measure, because of the hazard of perforating a sac when a dissection is done upon the side opposite that from which it is approached, usually the left, which has convinced us that this dissection on the opposite (right) side of the neck of the sac can be done with greatest safety and very much greater completeness in the second stage of the procedure when the small, troublesome veins in the neck of the sac are thrombosed, when the covering muscle fibers are edematous and can easily be wiped away, when the mediastinum and fascial planes are safely walled off, and when infection of the fascial planes or mediastinum, if it should occur from perforation, will not produce serious results.

We do not wish to be inordinately vain about this mortality rate of 2 deaths in 365 pharyngoesophageal diverticula, in all types of individuals, good risks and bad, at all ages, young and old, in all types of sacs, small and very large, adherent to the pleura and free, but it is a most convincing factor, at least to us, in our choice of and persistence with the two stage procedure in the treatment of patients with esophageal diverticula. The comparison of these two operative methods on the basis of mortality rates is a severe, but nevertheless a just one. If the series is large enough in this comparison, there is probably no more coldly fair method of comparing one type of operation with another than the mortality figures. In any series of one stage operations in which the mortality rate is higher than in the two stage procedure, the much discussed statement that it saves time has little appeal to the patient who dies, and all other comparisons such as decreased recurrence rates have little appeal, for in this series recurrences are really not decreased (12 recurrences in 250 cases or 4.8 per cent). Any type of operation is not satisfactory if there is another equally adequate one in which there is less chance of dying. Although it is true that a few sets of figures have been presented by men who have had a large experience with this lesion, in which the mortality is nearly comparable, there are none in a series of adequate size in which mortality rates following employment of the one stage method are as low as those here presented. With this in mind, it is impossible to make a just comparison of the two methods from the point of view of mortality rates unless the compared series consist of a minimum of 100 cases. Such is the variation in the ease with which pharyngoesophageal diverticula can be managed surgically that any study or conclusions drawn from a group of less than 100 cases is bound to be of inadequate value. We know of no surgical procedure which can be easier than that for the occasional pharyngoesophageal diverticulum of moderate size, or even quite large, devoid of peridiverticular adhesions, easily delivered and the patient in good condition, with a long thin neck and with fascia planes which separate easily. Likewise, we know of no operation which can be more complicated than the dissection of a pharyngoesophageal diverticulum in a patient with a short, thick neck, with a sac, large or small, thickly covered by cricopharyngeal muscle fibers, densely adherent either to

the mediastinum or the mediastinal pleura and with the sac likewise fused where it descends into the mediastinum, with its parallel-lying esophagus. We know of no operation in which the anatomic structures can be more difficult to expose than in a patient with a pharyngoesophageal diverticulum associated with an overlying or intrathoracic goiter. We know of no operation which can be more disturbing from the point of view of accurate dissection of the neck of the diverticulum than in the diverticulum, covered, particularly at its upper angle, with a venous plexus of dilated veins. It is to be remembered in discussing the steps in this operation that the neck of a pharyngoesophageal diverticulum comes off, in most cases, in the exact median position of the posterior aspect of the junction of the esophagus with the pharynx (Fig. 1). It is to be remembered that at this point rotation of the neck of the sac for adequate delivery and exposure of both sides and the back is impossible in terms of accurate anatomic demonstration of the submucosa and mucosa of the sac and its covering of cricopharyngei and inferior constrictor fibers, particularly on the opposite side of the neck of the sac from the side on which it has been approached, because of the fact that the esophagus cannot be rotated at the pharyngoesophageal junction.

The next most important criterion in the comparison between one and two stage operative methods in the treatment of pharyngoesophageal diverticula is the recurrence rate. We have deliberately limited our follow-up series to 250 consecutive unselected cases in order to include only those cases in which sufficient time has elapsed, a minimum of 2½ years, to make recurrences possible, if they are to occur. There were 12 recurrences in the first 250 resections of pharyngoesophageal diverticula. This is an extremely fair presentation of the percentage of recurrences since it includes the earliest cases in which, in all probability, we did not do as adequate dissections of the neck of the sac and as complete removals of the sac, with ligation of the neck flush with the esophagus itself, as we now do. It will surprise both of the authors of this report if a follow-up a year or two from now of the remaining 115 cases reveals a recurrence rate as high as in the first 250 cases.

The third criterion in the comparison of the two stage with the one stage operation for pharyngoesophageal diverticulum is the morbidity. Morbidity following operations for pulsion pharyngoesophageal diverticula consists of fascial plane infections, cervical abscesses, mediastinal infections, sinus tracts leading to that portion of the esophagus in the neck or that portion within the mediastinum (Fig. 5a and b). Morbidity also consists of draining empyemic sinuses and of narrowing or stricturing of the esophagus at the point of ligature or suture of the sac neck. In our series, there has been 1 instance of narrowing of the esophagus as a result of overenthusiastic removal of the neck of the diverticulum, which necessitated doing a secondary plastic enlargement of the esophagus at the point where the neck of the diverticulum was ligated. This was successfully accomplished, with an excellent result persisting over years.

There has been a very limited number of cases in which leakage has occurred following second stage removal of the sac in the two stage procedure. In all but 2 cases closure occurred spontaneously without further surgery or without the need to institute a gastrostomy, and in only 1 of the 2 cases was surgical intervention necessary to obtain closure. In 1 of the very early cases, due, probably, to inadequate removal of the neck of the sac, as will be shown later in a description of why sacs recur (Fig. 12), a sinus tract down to the point where the neck of the sac was ligated persisted for 3 years and closed spontaneously. In a recent case (2 years ago) there was leakage following a second stage due to insecure ligation of the neck of the sac, with the development of a food pocket at the cricopharyngeal junction which required a gastrostomy. This resulted in uneventful spontaneous closure of the pocket in a relatively short time. Other than these two complications, there are no sinuses, there have been no instances of empyema, no cervical abscesses, and no mediastinal abscesses. In the 365 cases now done there does not exist a single persisting sinus, and

in all of these cases other than the 12 patients who have had recurrences, swallowing is normal and relief complete.

In comparing one stage operations with two stage procedures for esophageal diverticula, one of the arguments which has been used in favor of the one stage procedure for this condition is that there is a saving of time. While we have never been impressed by the time saving argument in any operation over that of lowered mortality and morbidity, we are certain from our experience that the number of days patients spend in the hospital or, after they have left the hospital, in close touch with the surgeon who has operated upon them is no greater and may even be shorter with the two stage procedure than with the one stage procedure. In the beginning of our experience with this lesion, the second stage of this two stage operation for pharyngoesophageal diverticulum was undertaken on the twelfth day. For a number of years now this has been changed, and the second stage is done on the seventh day. This change was made for two reasons. There is an adequate walling off of fascia planes and mediastinum by the end of 7 days, particularly when, at the first stage, a drain has been placed in the lower end of the neck to wall off the mediastinum. More important still is the fact that it is easier to reopen the neck 7 days after the first stage of the operation than at a later period. There is less oozing in the field and the demonstration of the sac and the dissection of its neck by wiping the sac out are much more easily accomplished at the end of 7 days than when the second stage of the operation is delayed until the twelfth day.

At the second stage operation a Levin tube is guided into the stomach before the sac is ligated, and is left in place, through which the patient is fed for 7 days. On the seventh day after the second stage operation, the tube is withdrawn and the patient is permitted to eat, to leave the hospital, and to go home any distance on the same day. Thus, he leaves the hospital 14 days after the original procedure was done. No indwelling tube is placed in the stomach after the first stage operation. The employment of this plan has not resulted in accumulation of mediastinal or cervical fascial plane abscesses. This departure from the hospital for home is permitted only when there is no leakage at the second stage. Leakage occurs only in rare instances and is, for the most part, due to not having tied the ligatures of the neck of the sac securely so that the stump of the sac will not slip through the ligature, or to having cut away the stump of the sac so closely to the ligature that the ligature slips and permits leakage (see "Technique").

We have inquired of one of the outstanding advocates of the one stage method who has completed an almost comparable series of cases as to how long his patients are kept in the hospital or in the neighborhood of the operating surgeon, and have been informed that the average stay in the hospital is 2 weeks, with up to another week under close observation after the patient leaves the hospital to make sure that drainage does not occur or that late mediastinal or cervical accumulation which will require drainage does not occur.

It can safely be said, therefore, that one stage procedures do not save patients either days in the hospital or in a hotel for observation over the period of time required by the two stage procedure.

TECHNIQUE

In discussing surgical procedures for this lesion, we have often said that the type of incision employed, such as in operations for the radical removal of the breast and in various abdominal operations, is largely a matter of individual preference. For example, whether stomachs are resected or gallbladders are removed through longitudinal incisions, oblique incisions, or transverse incisions is largely related to the surgeon's experience and satisfaction with these types of incision. In the matter of the type of incision used in operations for pharyngoesophageal diverticula, however, this choice based upon personal taste is less applicable. According to the literature, three types of incision are employed for the removal of pharyngoesophageal diverticula: (1) the typical goiter incision with the end of the in-

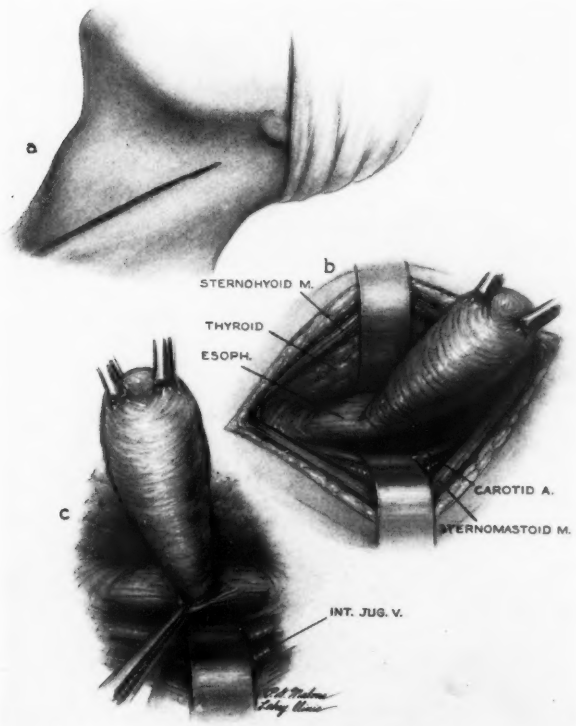


Fig. 8. a, The long longitudinal incision in front of the sternomastoid. In b, the wide exposure obtained by retraction of the common carotid, internal jugular, and sternomastoid; the thyroid gland is lifted out of the way by the second retractor. In c is shown in a semidiagrammatic way how the neck of the sac can be exposed in this wide and long incision. This drawing is a little misleading in that it suggests that the sac comes off the left side of the esophagus instead of the midline in the back, as mentioned in the text, but this distortion is necessary for the completeness of the exposure.

cision turned slightly upward on the left to make the approach to the pharyngoesophageal junction easier, (2) the transverse incision more or less in the folds and wrinkles of the neck directly over the region of the pharyngoesophageal sac, and finally, (3) the long longitudinal incision anterior to and paralleling the anterior edge of the sternomastoid muscle.

We have had many debates with advocates of the goiter type of incision and the transverse incision, but our choice has remained constant in the employment of the long longitudinal oblique incision in front of the anterior edge of the sternomastoid muscle. We are willing to admit that many of the small pharyngoesophageal diverticula could be approached quite satisfactorily with either the goiter or the transverse incision over the sac. Unfortunately, we have never been able to prophesy preoperatively before the exposure of the anatomy, which diverticulum can easily be exposed, delivered, and dissected and which will prove difficult. We have never been able to prophesy in which patient it would be easy or difficult to dissect the sac away from the esophagus, to free accurately all of its fibers at the inferior angle

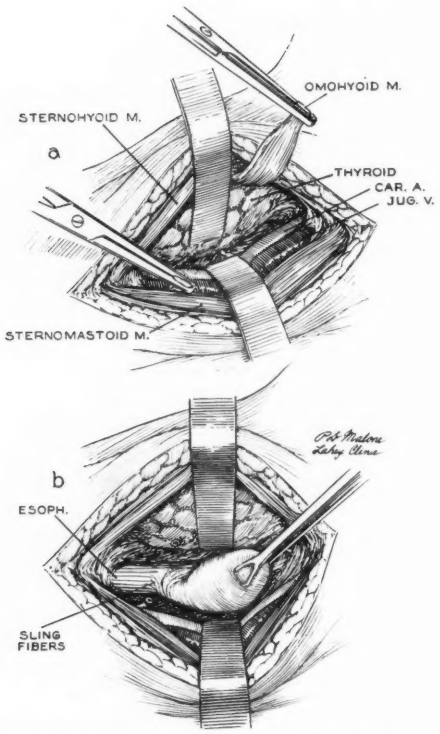


Fig. 9. In a, the first step in the removal of the anterior belly of the omohyoid is shown. Note that the tendinous portion has been clamped and cut. The anterior belly has been elevated and will be clamped and cut close to its insertion in the hyoid. Note also in this illustration, as stated in the text, the elevation of the thyroid, the retraction of the common carotid and internal jugular. In b, are demonstrated the sling fibers of the cricopharyngei together with the ligated and cut inferior thyroid artery at the lowest angle of the neck of the sac and the ability completely to free the neck of the sac as it joins the true esophagus so that when it is ligated it will be tied snugly against the esophagus itself in order that no neck may remain to produce another sac.

of the sac. We have never been sure when we would find an enlarged thyroid overlying the sac and its anatomic structures. Nor have we ever been able to be sure when the incision is being made in which operation for this lesion we will meet with technical difficulties such as bleeding, location of the recurrent laryngeal nerve, or such difficulties in exposure of the neck of the sac that they make us uncertain whether, in freeing all the fibers of the cricopharyngei from the neck of the sac, we had not unknowingly produced a small unrecognized hole in the sac, later to bring about serious fascial plane and mediastinal contamination. We are particularly anxious to make everyone aware of the need for exposure in those sacs of considerable size which have progressed into the mediastinum. We have more than once pulled an enveloping or adherent tongue of pleura up from the chest with the lower portion of the sac as it was dissected out of the mediastinum, an anatomic complication not easy to recognize, so fused can this pleural layer be with the sac of the diverticulum. We have more than once found, as the result of an inflammatory process about the lower end of the sac, the pleura and even the tip of the lung so adherent to the tip of the sac that its separation was extremely difficult—so difficult that it involved the decision as to whether or not it would be preferable to cut away the tip of the pleura and even the adherent tip of the lung, as has once occurred, or to risk cutting into the food and fluid-filled sac, with the resulting contamination of the mediastinal cavity. We have once accidentally opened the posterior parietal pleura, but in this case we were very glad indeed to have the wide anatomic exposure made possible by a longitudinal incision through which the pleura with its opening could be accurately exposed and closed.

We have appreciated the value of a longitudinal incision carried well above the level of the cricoid in those patients with a large plexus of veins so often present at the upper angle of the sac, near the superior thyroid artery and veins, difficult to control adequately enough so that a postoperative hematoma would not occur and often only adequately controlled after retraction or severing of the lowest fibers of the inferior constrictor. Such are the occasional hazards and difficulties in dealing with the numerous anatomic structures which must be met in this operation that the disadvantages of a long and less sightly scar are more than offset by the advantages of a wide exposure and the possibilities of accurate anatomic dissection (Fig. 8a, b, and c).

With the platysma cut, the skin flaps held back, and the anterior edge of the sternomastoid appearing and dissected free, the anterior belly of the omohyoid immediately becomes visible. This structure is accurately dissected and demonstrated, with control of all of the small vessels beneath the anterior belly, some of which are venous in character and some associated with the superior thyroid artery. The anterior belly of the omohyoid is caught between clamps, cut, and removed (Fig. 9a and b). It is important to carry the dissection well up to the attachment of the omohyoid to the hyoid bone since the outer edge of the thyrohyoid will then be exposed as it runs up with the omohyoid to be inserted into the hyoid bone. This is important because it is to this edge that the tip of the small and moderate sized sac is to be sutured at the first stage operation with 2 black identifying stitches, where it will remain between the first and second stages of the operation.

The advantages of removing the anterior belly of the omohyoid are very great. This immediately exposes the internal jugular vein with its branches running to the thyroid, and with this exposure these can be clamped and cut, freeing the edge of the thyroid gland so that it can later be turned up to expose the sac of the diverticulum behind it. It reveals the edge of the sternohyoid and sternothyroid muscles, which can be retracted forward. It exposes the middle and inferior thyroid veins running from the thyroid to the internal jugular, which can be severed and tied, and it exposes the outer edge of the thyroid which, as previously stated, can then be lifted up out of its bed with blunt retractors (Fig. 9a), the common carotid and internal jugular pulled back and the inferior thyroid artery, shown in Figure 9a, beneath which the sac of the diverticulum runs, can then be readily demonstrated. With this exposure the course of the recurrent laryngeal nerve can be felt for and the nerve demonstrated. The inferior thyroid artery, since the sac runs under it, is then severed between clamps and doubly tied (Fig. 9b). This exposes the region of the pharyngoesophageal diverticulum, which can

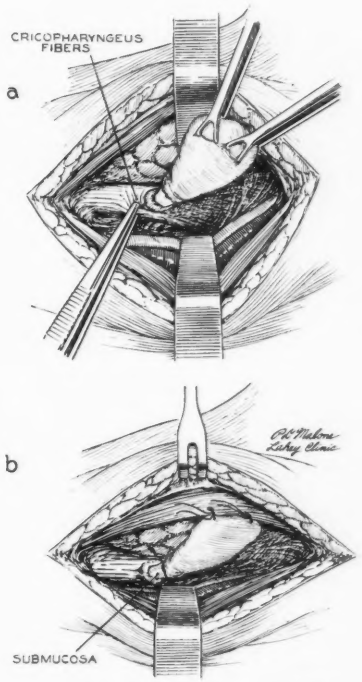


Fig. 10. a, This illustration in a semidiagrammatic fashion shows the neck of the sac completely freed of muscle fibers and consisting solely of mucosa and submucosa. This complete dissection all around the neck of the sac can, in our opinion, be safely accomplished only at the second stage. Note also the sling fibers demonstrated at the lower angle of the neck of the sac. b, The neck of the sac is completely dissected above, in front, and below, but the posterior layer of muscle is still unremoved, to be left to the second stage. Note also that this illustration in which the tip of the sac is fixed to the edge of the sternohyoid between the first and second stage gives the impression that the sutures pass through the wall of the sac but in reality they include only the adventitious tissue at the tip of the sac. Great care is exercised that the needle actually does not penetrate the wall of the sac because, as stated in the text, if it does leakage and soiling will be produced.

be separated in its fascial planes, prethyroid and prevertebral, so that the sac can be picked up and the junction between the inner edge of the sac and the esophagus demonstrated. The back of the sac and the esophagus can then be freed and the fascial plane, represented by the prevertebral layer of fascia, demonstrated. The dissection of the sac from its position parallel with the

esophagus itself or from within the mediastinum if it be large, can be carried out under good light and good anatomic exposure. When the sac is in the mediastinum, it is picked up with Babcock forceps and pulled up gently, replacing the Babcock forceps lower and lower as it is dissected free and delivered from the mediastinum until the entire sac is either out of the mediastinum if it be large, or dissected from below upward from the esophagus itself if it be of medium or small size. The extent of envelopment of the sac by the fibers of the cricopharyngei will vary greatly with different individuals. The investment will be thin and sketchy in some sacs and in others it will require very painstaking and accurate dissection with scissors to separate the diverticulum from the esophagus to which it has become adherent laterally and over which the fibers of the cricopharyngei envelop it. Once the sac has been liberated so that it hangs by its neck, it will still be completely covered by an investment of the muscular fibers of the cricopharyngei. In order to dissect the neck of the diverticulum so that at the second stage it can be accurately tied flush with the esophagus itself, and in order to prevent leaving a small section of the sac attached to the esophagus to bring about recurrence, it will be necessary so completely to dissect all of the cricopharyngeal fibers over the neck of the sac that the pale white submucosa of the mucous membrane lining of the sac will become clearly visible throughout the anterior, superior, and inferior circumference of the sac. Unless this is done one cannot be sure that the neck of the sac has been dissected completely free.

It is at this point that we wish to stress the fact that in our opinion it is impossible in a one stage or a two stage procedure at the first stage to safely dissect the cricopharyngei investment fibers from the back of the neck of the sac so that one can be sure that the front, the top angle, lower angle, and particularly the back of the sac are completely freed from these fibers and that the entire neck of the sac consists only of mucosa and submucosa, as shown in Figure 10a and b. Much of the discussion of the value of the one stage as opposed to the two stage operation for pharyngoesophageal diverticula in no way concerns itself with the accuracy with which this freeing of the neck of the sac of all muscle fibers with either method can safely be done; and almost none of the discussion of the one stage versus the two stage operation for pharyngoesophageal diverticula relates itself to the inadequacy of the safe exposure of the posterior aspect and right side of the neck of the sac since particularly the right side of the neck of the sac cannot be rotated to obtain this safe exposure, owing to the fixation of the upper end of the esophagus at the cricopharyngei junction. The hazards of carrying out such a blind dissection in a one stage dissection of the right side of the sac neck when it is approached from the left side, with the consequent danger of unrecognized perforation of the unvisualized sac neck, have never, we believe, been adequately discussed. One of the very great advantages of the two stage operation over the one stage operation for pharyngoesophageal diverticulum is concerned with this aspect of so completely freeing the neck of the diverticulum from its covering muscle fibers on the posterior and right side of the neck of the sac with safety that it can be ligated close to the esophagus, as is the sac of an inguinal hernia, so that the danger of recurrence is largely obviated. In a description of the freeing of the neck of the sac from its enveloping cricopharyngei fibers (Fig. 10a) in the two stage operation we want particularly to stress that the fibers in the exposure of the reverse side of this white submucosa at the neck of the sac are demonstrable directly under vision only at the lower angle of the sac, on the front of the neck of the sac, and at the upper angle of the sac. The dissection of these muscle fibers posteriorly and on the right side of the sac neck should be left for the second stage of the two stage operation when the small veins which bleed and ooze so exasperatingly at the upper angle of the sac are thrombosed, when the undissected muscle fibers on the back and on the blind right side of the sac neck are edematous and permit their being easily wiped away until the white submucosal layer, now edema-

tous and thickened, is easily exposed, and when, if perforation should occur and be unrecognized in this blind area, serious postoperative effects from contamination would not occur. If we were asked the outstanding advantage of a two stage procedure in this operation with which we have had such a large experience, we would not at once say its low mortality, but would stress the safety and the ease with which the posterior and right aspect of the neck of the sac can be freed from the overlying fibers of the cricopharyngei as compared with the hazards of this dissection in a one stage procedure if this complete freeing is done. If one assumes the position that the accurate removal of all of the cricopharyngei fibers and complete demonstration of the true neck of the sac with its white submucosa layer are unnecessary and that the sac neck can be ligated with these muscle fibers still unremoved without adding to the danger of recurrence, then this demonstration of the true sac and its accurate ligation on the esophagus are not necessary. In any comparison of the two methods, a good follow-up study of recurrences, as reported in this paper, is necessary as the comparison is likely to be done on a basis of mortality statistics only.

In discussing the surgical treatment of esophageal diverticulum, the mistake is often made of assuming that the neck comes from the left side of the esophagus. This assumes that the back of the neck of the sac can be readily seen, and in such articles illustrations are frequently shown with an accurate transfixion ligature at the cricopharyngeal junction. Such is not, in reality, the case. In a majority of instances a pharyngoesophageal pulsion diverticulum comes off directly in the midline of the back of the esophagus at the junction with the pharynx, at a point where the esophagus, as already stated, cannot be rotated since the cricoid and pharynx are fixed structures. It is to be remembered that just as the sac is invested with cricopharyngei fibers on the left, superiorly, inferiorly, and anteriorly, so it is invested on the right and posterior aspect where it cannot be brought into view, behind and to the right of the esophagopharyngeal junction, as shown in Figure 11. This freeing of the sac from behind

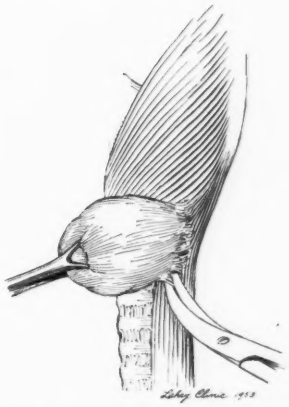


Fig. 11. In this diagrammatic illustration an attempt has been made to demonstrate the sac with its neck freed of the muscle fibers anteriorly, superiorly, and inferiorly, but when the sac is rotated to the right, the posterior fibers adherent to the esophagus are demonstrated. It is these fibers behind the neck of the sac that can in our experience only in the second stage be dissected accurately and safely so that mucosa and submucosa alone remain when the dissection is completed. Unless these fibers on the right posterior side of the neck of the diverticulum are completely freed, when the neck is ligated there is danger of leaving a portion of the sac to promote a recurrence.

the esophagus and on its right and posterior aspect through an incision in the neck on the left is a procedure in which are involved the hazards of lack of safe exposure and lack of certainty as to whether or not the neck of the sac is perforated as the muscle fibers are dissected from this portion of the sac neck. It must be remembered that when the cricopharyngeal muscle fibers overlying the neck of the sac are dissected free at the first stage operation, difficulties are encountered that are largely absent when this is done at the second stage operation. The overlying muscle fibers at the first stage operation do not separate easily from the underlying submucosa and mucosa, and there is often disturbing oozing from the plexus of veins on the esophagus at this point which does not permit safe identification and separation of submucosa and mucosa from muscle fibers without some hazard of inadvertently opening the mucosal and submucosal layers.

It will undoubtedly be said by many supporters of the one stage procedure that it is

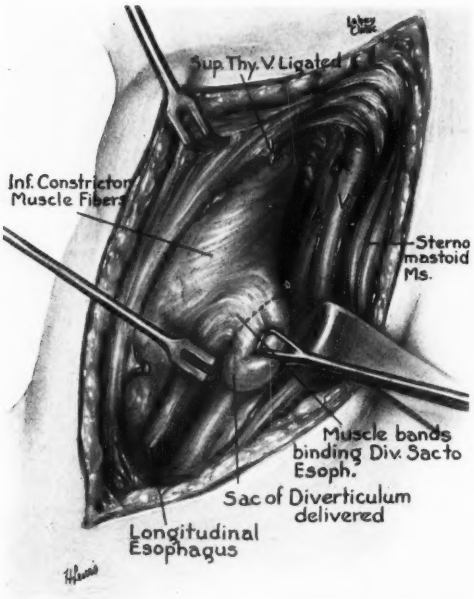

Sup. Thy. V Ligated
Inf. Constrictor Muscle Fibers
Sterno mastoid Ms.
Muscle bands binding Div. Sac to Esoph.
Sac of Diverticulum delivered
Longitudinal Esophagus

Fig. 12. In this illustration an attempt has been made to demonstrate that if all of the muscle fibers are not dissected from the neck of the diverticulum, if the lower angle of the sac as it is attached to the esophagus is not completely freed, indicated by the dotted line, a portion of the sac will remain to promote a recurrence.

not necessary to dissect these fibers from the neck of the sac as accurately as is here described but, as shown in Figure 12, this is not a fact because if all of the fibers of the cricopharyngei are not so accurately dissected from the inferior angle or right posterior aspect of the sac, there remains the beginning of another sac to promote recurrence. Accurate ligation of the neck of the sac (see Fig. 10) so that all of the sac is completely removed is possible when the entire neck of the sac consists only of submucosa and mucosa throughout its circumference.

As these dissections are made so that they demonstrate the pale white submucosa of the sac, as shown in Figure 10, it will be possible to see the fibers of the cricopharyngei directly beneath the lower angle of the neck of the sac, acting, as one of us (F.H.L.) has described, as sling fibers. It is important in this dissection that these sling fibers be elevated between the jaws of a small right angle clamp and so severed that no muscle fibers remain about the neck of the sac to promote a recurrence (Fig. 10a) and so that the tie about the neck of the sac at the second stage operation can be made close to the esophageal wall so that no sac can be left behind to promote a recurrence (Fig. 11). Anything short of this care concerning complete removal of the sac is comparable in inadequateness to inadequate removal of an inguinal hernial sac.

With all of the neck of the sac accurately dissected, the tip of the sac is now demonstrated. The fibers of the cricopharyngei or adventitious tissue about the tip of the sac are picked up with two hemostats, care being taken never to include in the jaws of the clamp the wall of the sac itself (Fig. 10b). The external edge of the sternohyoid close to its insertion is demonstrated, 2 black silk stitches are tied about the tissue included in the hemostats, a needle is passed through the outer edge of the sternohyoid and both black silk sutures are tied, as shown in Figure 13, attaching the tip of the sac to the outer edge of the sternohyoid muscle at a point well above the level of entrance of the neck of the sac into the esophagus. The 2 black silk stitches are cut long and laid on the anterior surface of the sternohyoid muscle where they can easily be found at the second stage operation and direct one readily to the position of the tip of the sac so that it can be picked up with tacking forceps as the sac is freed for final dissection and ligation. It is extremely important that no needles be passed through the wall of the sac as it is attached to the edge of the sternohyoid muscle since such a perforation will bring about leakage and contamination of the wound and make the second stage a much more difficult matter.

In large sacs, all of these steps of complete dissection of the neck of the sac will be possible, but the size of the sac will be such that it cannot be contained within the wound itself. In such instances the sac is implanted in the wound, taking care to place it high enough in the longitudinal incision in the neck so that the sac inclines upward to discourage the entrance of food into it.

At this point, the first stage of the operation is completed, a cigarette drain is placed in the fascial planes of the lower angle of the wound or into the mediastinum if the sac is large, and the platysma fibers are closed with catgut and the wound sutured (Fig. 13b).

Until a few years ago, the interval between the first and second stage operation was 12 days, but now for some years this has been cut to 7 days, since it has been found that the sac is well healed into the wound in this time and the fascial layers well walled off with granulating tissue. At the second stage, the sinus tract of the drain which is removed on the fourth day following the first stage is grasped on either side with double hooks as shown in Figure 14a, and the wound is gradually pulled apart, with a finger inserted along the sinus tract in front of the great vessels and upward to the top of the incision. It is to be remembered that there will be a well established line of separation through which the first stage operation has been done, represented on the outer side by the common carotid and internal jugular vein in one plane and on the inner side by the thyroid, the trachea, and the esophagus in the other plane. These are gently separated and pulled back. Thyroid pole retractors are placed over the internal jugular and carotid and pulled outward. A double blunt retractor is placed over the thyroid (Fig. 15a) and that structure is lifted upward and inward, resulting in exposure of the region of the esophagus and the region where the dissection was done in the first stage and the sac sutured at its tip to the outer edge of the sternohyoid muscle.

With the wound open and the outer edge of the sternohyoid muscle demonstrated, the 2 black sutures can readily be found resting on the front surface of this muscle, the sac detached by cutting the stitches, and its neck carefully wiped out with a small wad of gauze in a right angle clamp. The layer of cricopharyngeal muscle fibers over the posterior aspect of the neck of the sac can then be seen as a thick edematous layer and can easily be separated from the submucosa, severed, and wiped back. The sac will then be freely movable and its neck will consist throughout its entire circumference (top angle, bottom angle,

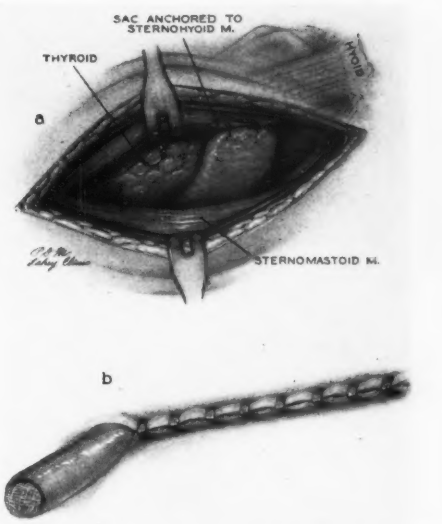


Fig. 13. In a is shown again the attachment of the tip of the sac to the edge of the sternohyoid. Again, comment must be made that this illustration is a little misleading and suggests that the needle has been passed through the sac when in reality it includes only the adventitious tissue about the sac. As previously stated, care must be exercised lest the wall of the sac be pierced by these 2 stitches, leak, and produce contamination. In b is shown a cigarette drain introduced at the lower angle of the wound into the mediastinum or into the lower part of the neck and wound closed with clips.

front neck, and back neck) only of submucosa and mucosa. The diverticulum is pulled out into the wound so that the mucosal and submucosal neck of the sac, now completely free of musculature, is put upon the stretch for accurate ligature (Fig. 15b). A No. 0 chromic catgut can be placed about the neck of the sac, the front portion of the ligature being held accurately against the esophagus at the neck of the sac and so tied that there will be no possibility of a sac being left, from which a recurrence can develop. It is important that the assistant hold the anterior segment of the encircling tie of the neck of the sac in front well against the esophagus itself so that one can be sure that all of the sac is included, the knot being tied on the right side of the neck of the sac to insure adequate inclusion of the neck of the sac on this side. It is here that the severing of the so-called sling fibers of the cricopharyngeal muscle at the

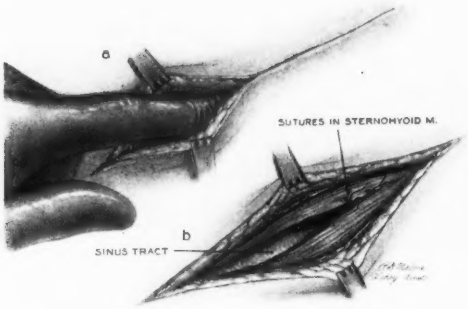


Fig. 14. In a is shown the edge of the wound at the second stage, done at the end of 7 days, grasped with double hooks, pulled apart, and separated by the fingers. At the end of 7 days this can be done with very little oozing and with practically no difficulty. In b is shown the wound further separated and the 2 black silk stitches anchoring the tip of the sac to the edge of the sternohyoid muscle beginning to appear. In the lower end of the wound is the sinus tract left by the drain shown in Figure 13b. These black silk stitches promptly indicate the position of the anchored tip of the sac and make it readily available to be grasped when the stitches are severed and the neck of the sac dissected.

first stage operation is so important as this permits pulling of a good section of mucosa out of the esophagus for ligature (Fig. 16). In many descriptions of ligature of the neck of the sac, particularly in those operations done in one stage, we have noted that transfixion of the sac is employed to prevent slipping of the ligature from the neck of the sac. This, we know, is unnecessary and undesirable since if the dissection has been so complete that the sac neck consists only of submucosa and mucosa, this will be a delicate structure and there will always be danger of tearing the transfixion suture at the neck of the sac, with the hazard of contamination. If the muscle fibers have not been removed there will remain a firm structure representing the neck of the sac which can, with reasonable safety, undoubtedly be transfixed, but in our experience this has been unnecessary. As we have already suggested, this may indicate, however, that the neck of the sac, as long as the muscle fibers about its neck are undissected and the sac does not consist solely of submucosa and mucosa, represents an inadequate dissection and so promotes an inadequate ligature of the neck of the sac close enough to the esophagus to insure against leaving a part of the sac behind, favoring another recurrence.

Based upon our experience, we would like to warn that after the neck of the sac has been ligated, because of the natural fear of leaving behind too large a rosette of ligated mucosa and submucosa which must die and be absorbed, there will be a tendency on most everyone's part to cut the neck of the sac off too close to the tie. This can and has in our experience resulted in slipping of the neck of the included mucosa through an inadequately tightened tie, leaving an aperture on the posterior aspect of the esophagus in a position which is almost impossible to close accurately, particularly if the dissection of the neck of the sac has been complete. We have had no hesitancy in leaving a good-sized rosette of sac neck, cutting off the neck of the sac at least ¼ to ⅜ inch from the point where the ligature surrounds it. In cutting off the neck, a right angle clamp (Fig. 16) is placed across the neck to prevent spillage of the contents of the sac into the wound.

If the neck of the sac is large, as it is with sacs of considerable size, it is closed by an open inverting chromic catgut stitch brought back to reinforce the inversion with a second layer (Fig. 17).

After the neck of the sac has been ligated, its cuff of ligated mucosa is gently pushed back under the esophagus to rest at the point where it originates behind the esophagus at the junction of the cricoid and the esophagus. A small amount of sodium sulfathiazole is placed over the cuff of mucosa behind the cricopharyngeal junction, a step which we think has become a habit and is not a necessity. A cigarette drain is placed in the mediastinum, to be removed on the fourth day. The wound is closed in layers. An indwelling Levin tube is passed through the nose as soon as the neck of the sac is exposed at the second stage to make sure that it enters the esophagus itself and can be passed well down into the stomach for feeding, and to make sure that it does not enter the sac and curl up in it. The patient is fed through the Levin tube for 7 days, only sips of water to wet the mouth being permitted, with the request that they not be swallowed. On the

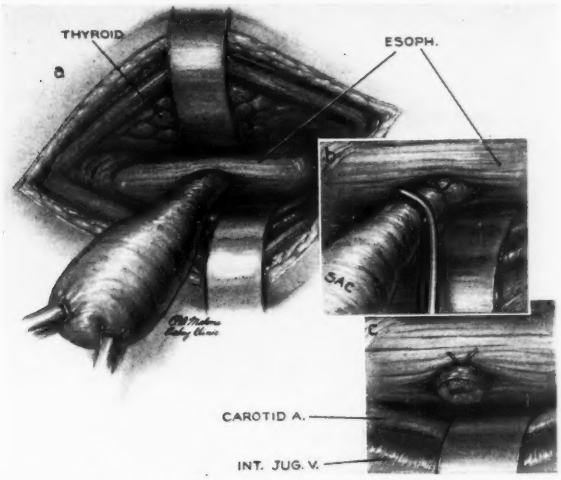


Fig. 15. In a is shown the exposure of the neck of the sac at the second stage. The origin of the sac is in the midline directly behind, and not as appears in this illustration coming off the left wall of the esophagus. This distortion is necessary in order to depict the actual exposure of the neck of the sac. In b is shown, again with the same distortion with the neck of the sac to the left, the accurate ligature of the sac neck level with the esophagus itself. The right angle clamp is placed at a proper distance from the ligature to prevent soiling of the wound from the contents of the sac. In c is shown the neck of the sac severed. Note that an adequate amount of sac neck still remains so there is no danger of the ligature slipping (see text).

seventh day the tube is withdrawn, the patient is permitted to eat and drink and is discharged from the hospital to his home, at whatever distance, on the same day. There have been no instances of leakage after these patients have left the hospital and returned to their homes.

We have had so much experience with esophageal diverticula of large size, and so with necks of the sac of such large character as to have required inversion suture with the esophagus open to bring about satisfactory closure, that we have frequently worried about the risks of contamination as the result of spilling of the sac or esophageal contents into the wound as the open esophagus has been closed. We used to be particularly worried about such contamination in the presence of a widely opened mediastinum. With delayed second stage closure by suture of such large openings into the esophagus, even when a large mediastinal cavity is left by the removal of a large mediastinal sac, we have had no difficulty and no instances of infection, due, we believe, to the walling off of granulations in the mediastinum at the second stage.

In the management of large intrathoracic pharyngoesophageal diverticula in the first stage of the operation, as shown in Figure 18a, we have for several years not found it necessary to employ preliminary gastrostomy to build up these patients. In those patients, as shown in Figure 18b, who have lost large amounts of weight, we have, following the complete freeing of the sac, introduced a Levin tube through the tip of the sac by means of a purse-string suture, guided the tube down into the esophagus itself and on into the stomach so that the patients may be fed immediately through this tube during the interval between the first and second stages of the procedure. This has proved a very valuable method of improving the condition of these patients between the first and second stages, and of avoiding a gastrostomy. We have, with this plan, seen weight gains of 8, 9, and 10

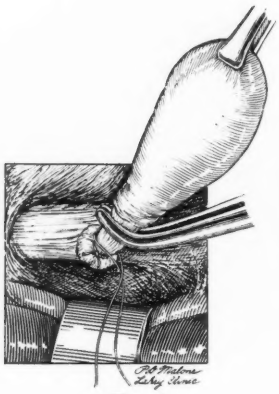


Fig. 16.

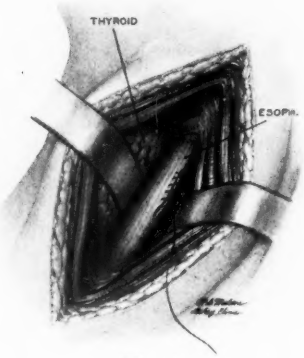


Fig. 17.

Fig. 16. This illustration again demonstrates the complete dissection of the neck of the sac so that only mucosa and submucosa remain, and the true position from which the neck of the diverticulum sac springs. Note the additional precaution frequently employed of doubly ligating the neck so that the danger of slipping and leakage is avoided. Note also the safe margin of sac between right angle clamps and the ligature to prevent slipping of the ligature.

Fig. 17. In this illustration is diagrammatically depicted the suturing of the neck of the sac over and over and inverting it with a return stitch in those patients who have a very large diverticulum with the neck too wide for safe ligature. If ligatures were employed in the neck of the sac of very large diverticula they would so constrict the esophagus that an obstruction could be produced.

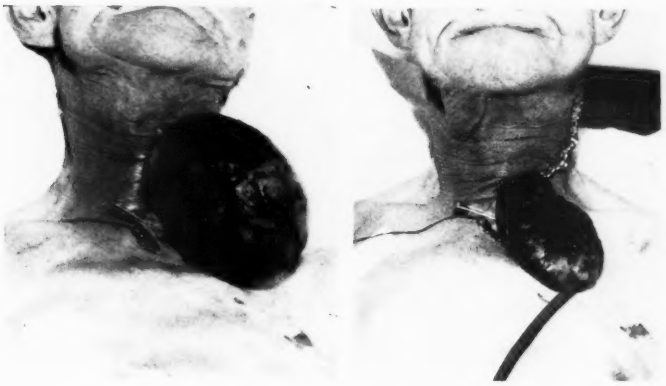
pounds in markedly emaciated individuals in this short period of 7 days.

Wound closure in the second stage is similar to that in the first stage, and there have been no difficulties with contamination in these reopened wounds. In cases in which large mediastinal cavities remain, a rubber catheter drain must be kept in place until the cavity has become closed by expansion of the pleura.

OPERATIVE COMPLICATIONS

In discussing the surgical management of pharyngoesophageal diverticulum it is important not only to discuss the technical measures employed in their removal but also to mention some of the complications which have arisen in the course of these operations and how we have met and dealt with them.

As has already been stated in the description of the operative method, so long-standing will be some of these esophageal diverticula and so many times as the result of irritation and infection within the sac itself will there be adherences of the sac to the pleura and surrounding structures deep in the mediastinum that this will be a serious problem to deal with at the time of the first operation. In addition to this, such will be the progress of these deep sacs into the mediastinum that as the sacs are delivered from this deep position, good-sized sections of pleura will sometimes be adherent to the tip or back wall of the sac, and as the sac is pulled out of the esophagus, a not inconsiderable section of such pleura adherent to the sac will come out of the mediastinum with it. It is important as these deep sacs are delivered from the mediastinum to inspect the tip and lowest posterior walls of the sac very closely under a good light to make sure that the tissue adherent to the sac at these points is not a tongue of the parietal or apical pleura. Once demonstrated, the adherent pleura can usually be separated without opening it by dissection from the sac wall when the line of cleavage between these two layers to the tip of the sac is apparent. The thickened plaques of inflammatory tissue sometimes so involve the tip of the sac, the



a b

Fig. 18. a, This illustrates a method previously employed in a complicated diverticulum of such size as to interfere with swallowing. b, The method of decompressing a sac of such size filled by swallowed air and also the method of passing a tube through the sac into the esophagus and so on into the stomach for feeding are demonstrated.

pleura, and occasionally the apex of the lung is to raise a problem as to how to handle them. In 1 such case the decision had to be made whether the inflamed and adherent plaque of pleura should be severed away from the wall of the diverticulum to which it was adherent and of a thick-walled character, or a section of the sac should be cut away and left adherent to the pleura, with the risk of contamination from spilling of the contents of the sac, a dangerous complication in the first stage operative procedure. The former decision was made, that is, to excise the pleura, with the idea that the pleura could be closed if necessary. On severing such a plaque it was found that the tip of the lung was adherent to the sac and required removal with the adherent section of the pleura, and the open and adherent alveolar spaces of the lung could be plainly demonstrated. The cavity in the mediastinum was packed with wet gauze. For a few days the neck became emphysematous but the fistula into the alveolar spaces soon closed uneventfully.

In another not unsimilar case, the parietal pleura from the back wall of the thorax, to which the sac had become adherent, was pulled up with the sac, not recognized, and opened. As the result of this experience we now know that sometimes such parietal pleura can be demonstrated to possess a thin layer of adipose tissue adherent to it which serves to identify it, and this, in another case, would suggest to us in the dissection that we were dealing with the parietal pleura, and cause us to separate more carefully the line of cleavage between such a parietal pleura and the adherent apex of the sac.

In 1 instance in this series, at the second stage operation we were confronted with a torn internal jugular vein in a wound which was granulating and oozing, and an accurate dissection of the internal jugular vein from the common carotid was obviously not possible. This was successfully dealt with by an incision posterior to the sternomastoid and the demonstration in a clean, uninvolved field, of the internal jugular at a point above and below the point of tear, with ligature of the internal jugular above and below, without complications.

In operating upon recurrent diverticula, our own cases and those sent to us, we have in 5 cases made openings in the delicate sac in the course of a dissection made difficult by the adhesions of the sac to the prevertebral fascia, larynx, or thyroid as a result of the previous operation. When such a small hole can be demonstrated in the delicate neck of the mucosal sac, we have found it much superior

Fig. 19. Roentgenogram of epiphrenic esophageal diverticulum of moderate size.

to pick up the tissue about the small hole with a delicate hemostat, hoist it, twist it, and ligate it away from the opening rather than to try to close it with stitches, because the passage of the needle through the delicate mucosal opening so increases the size of the opening in the sac that it cannot be closed successfully.

We have twice in the course of a first stage dissection demonstrated, in an accurate dissection of the neck of a small sac, that a small opening had been made in the neck of the sac, and we have unhesitatingly converted this operative procedure into a single stage procedure, tying the ligature around the neck of the sac proximal to the hole. When diverticula are small, it is better to do this than to attempt to close the hole in the sac, implant it in the wound and proceed as with a two stage procedure, again because of the danger of leakage and fascial plane contamination.

Follow-up study in this series has revealed that the recurrent laryngeal nerve has been injured in 12 cases. Many of these injuries occurred in the early stages of our experience with this operation but are now avoided by feeling for the recurrent laryngeal nerve and pushing it against the trachea to demonstrate it or by dissecting and demonstrating the nerve when the inferior thyroid artery is tied.

In no instance in this series has there been an injury to the thoracic duct. It is unlikely that this complication will arise in the surgical management of this lesion since the dissection is carried on in a plane posterior to the location of this structure.

In 1 patient sent to us after an esophagoscope had been pushed through the sac, the neck had been opened by a long longitudinal incision and a gauze pack placed in the mediastinum at the point where the perforation had been made at the tip of the sac. When the patient entered the hospital one of the assistants gently started to remove the pack from the mediastinum, with the prompt occurrence of a massive venous hemorrhage from the mediastinum about the pack. He had the good sense to push the pack back into the mediastinum, with complete control of hemorrhage. The patient was taken to the operating room where, with a good light, good anesthesia, and good exposure, one of us (F.H.L.) pulled the pack a little way out of the mediastinum, with recurrence of the profuse venous bleeding. With gentle extraction of the pack and its quick reinsertion, it could be seen that the deep venous bleeding was from a hole in the wall of the internal jugular vein. This is an unusual complication but a description of the method of its control may be valuable to one in a similar position.

The jugular vein was dissected free from the carotid in the midneck and cut between clamps. The upper end was ligated and the lower end clamped and twisted until the twist in the vein passed the opening in the wall, thus controlling the deep bleeding. The pack was removed, a small right angle clamp was placed upon the twisted vein below the level of the opening in its walls and ligated, controlling this annoying and dangerous complication.

RECURRENCES

Most recurrences of esophageal diverticula of the pharyngoesophageal type are the result of incomplete dissection of the neck of the sac and so, incomplete removals of the sac (Fig. 12). As shown in the diagrammatic illustration (Fig. 4a), it can be seen that since the diverticulum descends parallel with the wall of the esophagus itself, it creates a sharp angle, often difficult to separate completely, and unless this angle is so thoroughly dis-

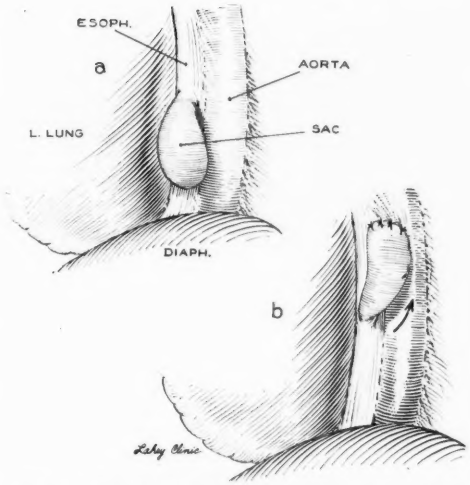


Fig. 20. In this illustration is shown a diagrammatic method of dealing with an epiphrenic diverticulum, a, by freeing the sac and, b, suturing it to the vertebral gutter parallel to the vertebral body to prevent the passage of food into the sac. In 3 such cases the results have been excellent. Today, with our ability to deal with these sacs transthoracically, this method is not recommended.

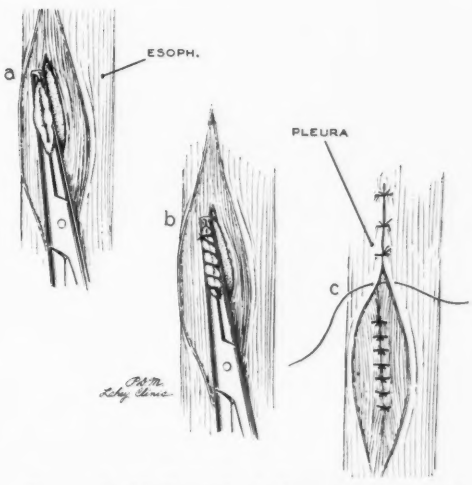


Fig. 21. In this illustration is shown the transthoracic method of dissecting the epiphrenic diverticulum completely, severing the neck between the clamps, oversewing the remaining sterilized segment of esophagus caught in the inner clamp, inverting the oversewed section of the esophagus with interrupted stitches, and closing the pleura over it with this suture line.

sected that no angle remains (Fig. 10), ligation of the neck of the sac with part of the wall of the diverticulum still adherent to the esophagus itself will promote recurrences. When the neck is ligated with the angle retained as shown in Figure 12, there will remain the beginning of a small sac which, with the shelf created by the adherent wall of the diverticulum to the esophagus to direct food into the sac, will bring about recurrence of another sac. This, we believe, is an extremely important point in the need for radical and accurate dissection of all of the neck of the sac if the complication of recurrence is to be avoided.

So thin and indefinite are the muscle fibers about the neck of the sac that employment of them to reinforce the ligated sac neck is largely impossible and, when possible, is of little value particularly if the neck of the sac is so dissected that only mucosa and submucosa remain.

EPIPHRENIC PULSION ESOPHAGEAL DIVERTICULUM

Little need be said about this lesion, first described by Zenker and Ziemssen in 1877.

The cause of epiphrenic pulsion diverticula is less easy to explain than are the causes of pharyngoesophageal pulsion diverticula. This lesion, in all probability, however, is the result of a weakness in the lower end of the esophagus which must be largely limited to this epiphrenic point because no lesions are reported in the literature of this type above this level at the lower end of the esophagus. It must also undoubtedly be brought about in somewhat the same measure as are pharyngoesophageal diverticula by cardiospasm or fibrosis and the occurrence of an increased intraesophageal pressure which results in the mucosa breaking through a weak point of the muscularis walls at this point.

In dissections of the necks of epiphrenic pulsion diverticula it has been noted by one of us (F.H.L.) that the wall of the sac is similar to that in the pharyngoesophageal diverticulum and the line of separation of the muscular fibers of the esophagus is readily demonstrable in the course of the accurate dissection of the muscle fibers from the neck of the sac. This lesion does not possess, as does pharyngoesophageal diverticulum, a relation-

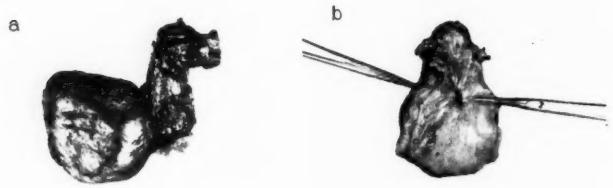


Fig. 22. a, A diverticulum which produced obstructive symptoms at the level of the entrance to the diverticulum. In b, note the smallness of the aperture leading to the epiphrenic sac and the degree of contraction of the esophagus at this level. This diverticulum required complete transthoracic resection of the esophageal segment involved together with the sac.

ship of symptoms to stages of development. In all of the cases with which we have dealt (9) there has been a true sac of globular shape (Fig. 19) and the complaints have been largely those of decaying food which had accumulated within the sac, which has produced a foul breath, the regurgitation of foul food contents of the sac, distaste for food and the resulting nausea.

Three of these 9 sacs have been successfully dealt with transthoracically by one of us (F.H.L.) by suturing the sac in the vertebral gutter parallel to the vertebral bodies (Fig. 20). The remainder have been dealt with either by resection of the remaining sac intrathoracically by the thoracic surgeons (1) of the clinic, oversewing the neck and inverting it into the esophageal wall by silk stitches through the muscularis, as shown in Figure 21. In 3 of these cases, such was the degree of obstruction that, as shown in Figure 22a and b, a complete transthoracic resection was necessary. There have been no fatalities and the ultimate results in all these cases have been satisfactory. This lesion requires much less discussion and has not attached to it any of the debatable differences of opinion that are involved in the surgical treatment of pharyngoesophageal diverticulum. With the advances made in thoracic surgery, the surgical treatment now accepted for these lesions consists either in resection of the neck of the sac and

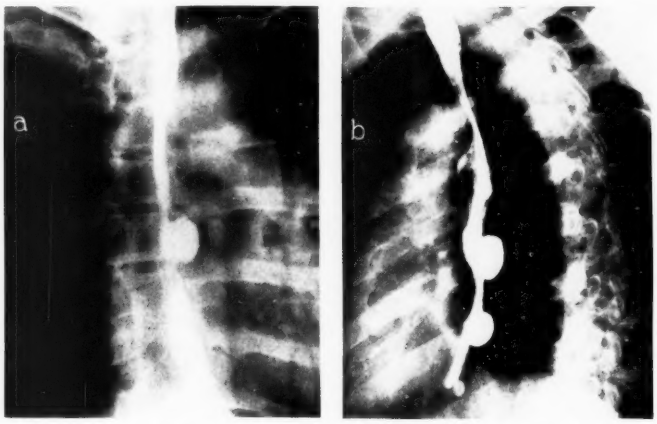


Fig. 23. a, A single traction diverticulum at the level of the main bronchi is shown. It is this type of diverticulum that rarely requires surgery and can be treated quite satisfactorily by dilatation. b, Multiple traction diverticula which can likewise be treated quite satisfactorily by dilatation.

inversion of its oversewn neck into the esophagus or in transthoracic resections of that portion of the esophagus involved when obstruction to the esophagus itself has occurred.

In Figure 21 is shown the method which one of us (F.H.L.) has employed in dealing with resections of such transthoracic sacs by applying 3 Ochsner clamps to the neck of the sac. The sac is cut away between the middle and distal Ochsner clamps, the middle clamp which has crushed the mucosa of the esophagus is then removed, the edge of the crushed esophagus sterilized with carbolic acid and the crushed neck of the sac oversewn with a continuous suture of catgut. The inner Ochsner clamp close to the esophagus is removed, the suture of the oversewn neck is pulled up tight, inverted, and pushed into the wall of the esophagus between the muscle fibers, and the muscle fibers of the esophagus are closed with interrupted silk sutures over the buried stump. There have been no mortality and no leakage in these cases.

TRACTION DIVERTICULA

Traction diverticula, as stated in the historical summary in the beginning of the article, fortunately rarely require surgery. Traction diverticula are true diverticula and may be solitary (Fig. 23a) or multiple (Fig. 23b). They possess all the muscular and mucosal coats of the esophagus. Due largely to contraction of inflammatory adhesions to the bronchial lymph nodes and occurring largely at the level of the main bronchus, they are rarely dependent in position. They are pulled transversely or in the upward direction by the inflammatory attachment to the cicatrizing and healing bronchial lymph nodes and are usually capable of emptying their contents. They are, for the most part, dealt with quite satisfactorily by dilatation when any symptoms are associated with them other than those of obstruction.

There will, however, be an occasional case in which the sac will be dependent and the same set of symptoms will then occur as occur with an epiphrenic pulsion diverticulum at a lower level. There will be occasional cases in which, as the result of the inflammation in the sac, there will be either obstruction of the esophagus which will require resection or a break through between the sac and the bronchus which will require separation and suture.

CONCLUSIONS

This paper includes a historical background of the occurrence and management of esophageal diverticula.

Its diagnosis and its separation from dilatation of the esophagus above an esophageal web by roentgen examination are discussed.

Its surgical management by the two stage operation is described and illustrated.

Some comparisons are made concerning the advantages of the two stage over the one stage operation.

The complications which have been encountered in this series, together with the mortality in a follow-up study of 250 of the patients operated upon for this lesion, are presented.

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AN ANALYSIS OF FORTY-NINE CASES OF SQUAMOUS CELL CARCINOMA OF THE ANUS

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SQUAMOUS cell carcinoma of the anus has not been studied as thoroughly as tumors elsewhere in the gastrointestinal tract. Accurate knowledge of its manner of spread and of many of its other characteristics is lacking. There is still much disagreement among both surgeons and radiologists as to how it should be treated and few statistical reports have been published of late results following treatment. This situation can be attributed in part to its infrequent occurrence and to the fact that it has been overshadowed by carcinoma of the rectum, which has been studied much more carefully and about which much more is known.

This series includes 49 patients admitted to the Presbyterian Hospital from 1916 to 1952 inclusive. Some of these patients were included in reviews by Raiford in 1933 and Harvey in 1946. Patients who received definitive treatment elsewhere and those who were treated in the out-patient department but were not admitted to the hospital were not included. Patients with tumors arising from the perineum, scrotum, labia, and buttocks and not primarily from the anal canal itself were also omitted. There were no squamous cell carcinomas in this series that arose primarily above the anal canal from the rectum or higher in the large intestine such as have been reported by Keyes, Cattell and Williams, and O'Brien and Meehan (16). Whether these higher tumors originate from embryonic rests, from the undifferentiated basal cells of the mucosa, or from metaplasia of the superficial cells of the rectal mucosa has not been determined.

Omitting 6 patients seen in 1951 and 1952, 43 patients with squamous cell carcinoma of the anus were admitted to the hospital from 1916 to 1950 inclusive. During the same period 2,341 patients were admitted to the hospital with carcinoma of the large intestine. Of these 1,026 had carcinoma of the rectum. Thus the anal tumors comprise 1.8 per cent of the combined anal and large intestine tumors and 4.0 per cent of the combined anal and rectal lesions, or a ratio of 1 to 24.9. This incidence is similar to that reported by other observers.

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Of the 49 patients in the entire group, 18 were men and 31 women. The average age was 57.9 years. This is similar to that of 56.7 years found in patients with carcinoma of the rectum in this hospital. The oldest patient was 94 and the youngest was 32. The ratio of men to women differs from the slight preponderance of males over females of 1.4 to 1 in our patients with carcinoma of the rectum.

The etiology of these tumors is, of course, not known but they have often been found superimposed on other lesions. Fistulas are the lesions most frequently mentioned as giving rise to them but leukoplakia, fissures, hemorrhoids, lymphogranuloma venereum, and irradiation have also been implicated as reported by Buie and Brust, Rosser (21,22), Binkley and Derrick (3), David and Loring, Cattell and Williams, and others. In 3 patients in our series the tumor appeared to arise secondarily to an anal fistula of long duration. In 1 of these patients the fistula had been present for 20 years. These fistulas should be differentiated from those of short duration that occasionally develop from infection about the tumor itself. In another patient the tumor apparently arose in a mucosal prolapse and in still another patient in a stricture caused by lymphogranuloma venereum.

The tumors were divided arbitrarily according to size into two groups, large and small. In the large group were 34 tumors comprising about two-thirds of the total number. These were annular or nearly so, approximately 3 by 3 centimeters or more in diameter, and extended upward into the rec-

Fig. 1. S. P. 77413. A well differentiated squamous cell carcinoma of the anus. ×95.

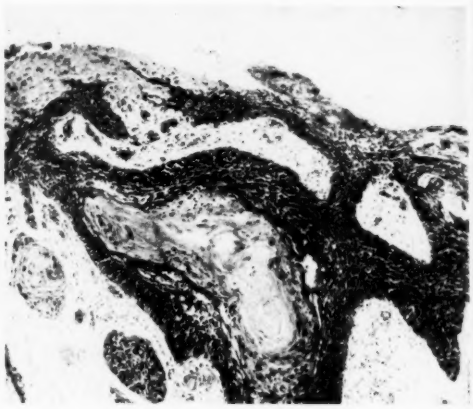

Fig. 2. S. P. 64687. A moderately well differentiated squamous cell carcinoma of the anus. ×95.

tum or laterally well out into the perianal tissues. Nearly all the tumors invaded the sphincter muscles and extended out into the perianal tissues to some extent. A surprising number spread upward into the rectum, occasionally as much as 6 or 7 centimeters. The small group comprised 15 tumors, about one-third of the total. They included the only case of intramucosal carcinoma in the series. There were too few cases for a comparison of 5 year results in the two groups.

The tumors were graded according to their degree of differentiation into three groups: well differentiated 17, moderately well differentiated 21, and poorly differentiated 7 (Figs. 1, 2, 3, and 4). Sections were not available in 4 cases. Because of the small number of cases no correlation could be shown between the degree of differentiation and late results following treatment.

Sixteen of these tumors had some of the histologic characteristics of basal cell tumors. Three of these had lymph node metastases. Grinvalsky and Helwig have recently suggested that these are not true basal cell epitheliomas but rather transitional cell epitheliomas which probably arise from the transitional cell lining of the anal ducts which have a common embryologic origin with the urethra and bladder.

Bleeding and pain were the commonest symptoms. There were also the most frequent initial symptoms. A local sense of mass was the next commonest. The average duration of symptoms was 7.8 months. In carcinoma of the rectum most authors record it as being from 9 to 11 months. Since the anal canal has greater sensory nerve innervation than the rectum, one would expect earlier response to pain and, therefore, earlier diagnosis.

The diagnosis was usually made from the presence of a mass or ulceration in the anal region which had been confirmed by biopsy. Errors in diagnosis were fairly common and could have been avoided if an early biopsy had been taken in each case. In 3 such cases the error in diagnosis caused serious delay in treatment. In 1 patient in whom the tumor developed in a stricture caused by lymphogranuloma venereum it was several years before the diagnosis was made. Another patient was operated on by her physician and treated for over a year for an anal fistula before it was discovered that the fistula was caused by an anal carcinoma. Another patient had 2 operations for periurethral abscess believed to be secondary to a urethral stricture before it was discovered that the abscess was secondary to a carcinoma of the anus.

TUMOR SPREAD

Local spread. Squamous cell carcinoma spreads by local extension, through the lymphatics and occasionally through the blood

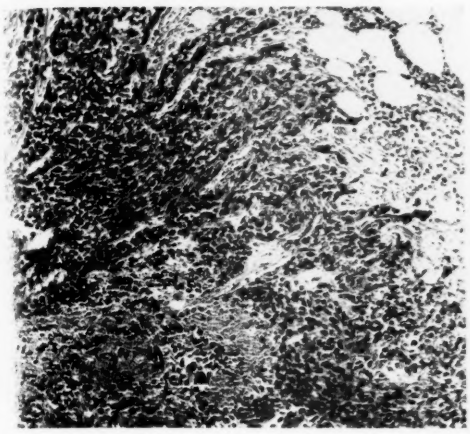

Fig. 3. S.P. A31646. A poorly differentiated squamous ll carcinoma of the anus. ×95.

Fig. 4. S.P. A28425. A squamous cell carcinoma of the anus simulating basal cell carcinoma of the skin. ×95.

ream. In this series local spread to the phincter muscles and perianal tissues was requent but extension to neighboring viscera ich as the prostate, vagina, and bladder was nfrequent and occurred only late in the disase. It was found in only 9 patients, involvng the vagina in 3 cases, the prostate in 3 ases, the bladder in 2 cases, the sacrum in 1 ase, and the cervix in 1 case.

Spread by the blood stream. Distant metasases presumably by way of the blood stream were rare. In only 2 (4.1 per cent) patients was the liver found to be involved. In both instances the involvement was discovered at autopsy. In none of our patients was clinical evidence of liver metastasis found during the course of the disease. There was no instance of metastasis to the lungs, spine, brain, or other distant areas. It must be remembered, however, that many patients were not seen during their terminal stages and autopsies were obtained on only 5. Carcinoma of the rectum, on the other hand, has shown a considerably higher incidence of distant blood-borne metastases. In 268 patients who underwent curative abdominoperineal resection in this hospital for rectal cancer from 1916 to 1945 inclusive and who either died of recurrent disease or survived 5 years, the incidence of liver metastasis found was 10.8 per cent (29 cases) and the incidence of metastasis to the lungs, spine, or brain was 7.5 per cent (20 cases). If patients with advanced disease who received only palliative treatment or none at all had been included, the incidence of such metastasis would undoubtedly have been still higher. Microscopic evidence of invasion of the veins by carcinoma cells was not reported in any of the sections of the anal tumors, whereas in a series of carcinomas of the rectum previously reported (8) the incidence was 36 per cent. It is, of course, true that the finding of vein invasion in microscopic sections depends largely on how thoroughly the search is carried out. Although in the rectal series the study was a much more careful one, there appears to be little doubt that vein invasion is less frequent in carcinoma of the anus. Keyes and Cattell and Williams have also stressed the rarity of blood-borne metastases, either to the liver or elsewhere.

Lymphatic spread. Metastases by way of the lymphatics occurred frequently. Involvement of the perirectal and mesocolic lymph nodes by the upward route along the inferior mesenteric vessels was found in 7 of the 25 specimens removed by abdominoperineal resection or perineal proctectomy. This is an incidence of 28 per cent. Nine of these specimens, or about one-third, were cleared by a modified Spalteholtz technique for study of the lymph nodes. Unfortunately, as most of

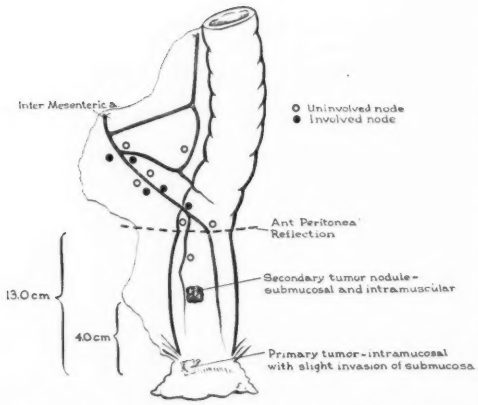

Fig. 5. S.P. A squamous cell carcinoma of the anus removed by abdominoperineal resection with metastases in 6 of 12 nodes found along the inferior mesenteric artery after clearing the specimen.

the specimens which showed metastases were not cleared, the site of the node metastases and the extent of upward spread was not determined. In a series of 245 specimens of carcinoma of the rectum similarly removed in this hospital from 1936 to 1945 inclusive, with clearing of 78 specimens, or about one-third, the incidence of node metastasis was 42.4 per cent (104 cases). The two series are comparable in that, in each, a similar proportion of specimens was cleared. The figures suggest that upward spread is less frequent in carcinoma of the anus. It was our impression also that the node metastases in tumors of the anus were usually grouped closer to the primary tumor and were less often found at higher levels than those in carcinoma of the rectum. The present series is too small, however, to warrant definite conclusions. Keyes believes that upward spread is frequent but does not extend to a high level. The accompanying drawing (Fig. 5) shows a specimen removed by abdominoperineal resection in a very recent patient who was not included in the series. After clearing the specimen, 6 of the 12 nodes found showed metastasis. Five of the involved nodes lay above the peritoneal reflection and 2 were not far from the point of ligation of the inferior mesenteric artery. At least 4 of the involved nodes would not have been removed by perineal excision and colostomy. No other metastases were found. Unfortunately, lymph node studies by the clearing technique have not been done on any large series of cases. It may be that upward spread is more important than has been believed.

Metastasis to the inguinal nodes has always been emphasized as one of the most frequent paths of spread in carcinoma of the anus. In this series, patients who underwent inguinal node dissection were divided into two groups, those on whom the excision was done at the time of their first admission to the hospital and those on whom the excision was done at a later admission. They were also grouped according to clinical evidence of involvement at the first examination. None of the dissections included removal of the iliac nodes. Removal of nodes at the first admission was only done on patients whose nodes were clinically enlarged. There were 13 of these patients, 7 had bilateral dissections and 1 unilateral. The unilateral excision was the only one in which a metastasis was found. This was a patient with such advanced disease that only a colostomy and palliative radiation were considered advisable. Inguinal node dissection was done at a later admission on 5 patients. In 2 of these patients metastases were found. A third patient developed local ulceration in the inguinal region which was apparently caused by metastatic cancer but no biopsy was taken. In all 3 patients the inguinal involvement was a late one, occurring 13, 28, and 38 months after their primary treatment. It is possible that some inguinal metastases, especially the late ones, are secondary to pelvic node metastases and may not represent direct lymphatic metastasis from the primary tumor. Only 4 (8.2 per cent) of the 49 patients in this series had evidence of inguinal metastases. Only 1 patient was found to have it at the first admission and his was an advanced case. The other 3 were also examples of late involvement. All 4 patients died of their disease within 4½ years of the time they were first seen. From this small series it would appear that inguinal metastasis is rather infrequent early in the disease and may constitute less of a threat than has been supposed. Other reviewers have found it more frequently. Sweet

reported 18 of 77 patients with inguinal involvement at the first examination, an incidence of 23.4 per cent. Sixteen of 23 patients in his series who died of recurrent carcinoma after radical surgery had inguinal metastases. In our series there was only 1 such patient of 6 similarly treated. Routine excision of the inguinal nodes following resection of the primary tumor has been advocated by Cattell and Williams, Bacon, and Pack and Rekers. They advise a radical dissection extending above the inguinal ligament to include the iliac nodes as well as the femoral and inguinal. Cattell also does an inguinal dissection as a palliative measure for relief of pain and to avoid ulceration. Gabriel and Binkley do not advise inguinal dissection unless the nodes are enlarged.

When all lymph node metastases were studied, including not only those found in the resected specimens and in inguinal node dissections as already mentioned, but also pelvic node metastases removed at operation and nodes examined at autopsy, they were found to be present in 11 patients or an incidence of 22 per cent. Two patients had upward spread to the perirectal and mesocolic nodes only, 1 patient had lateral spread to the pelvic nodes only, and 3 patients had inguinal node involvement only. Four patients had both upward and lateral spread, and 1 patient had metastases in all three groups of nodes. It is evident that metastases may occur by all three routes. Further studies may show that upward and lateral spread are of equal if not greater importance than inguinal. The importance of lateral spread is especially difficult to determine as the pelvic nodes are not ordinarily removed in the usual radical operation.

RESULTS OF TREATMENT

Figure 6 shows the number of patients treated by curative surgery and curative radiation from 1925 to 1952 inclusive, grouped in 3 year periods. Patients treated by palliative surgery or palliative radiation were not included. One patient treated by surgery with hope of cure and later by radiation at another hospital was also omitted. The first patient treated by curative surgery was operated on in 1925 and the first patient given radiation in dosages sufficient to offer hope of cure was

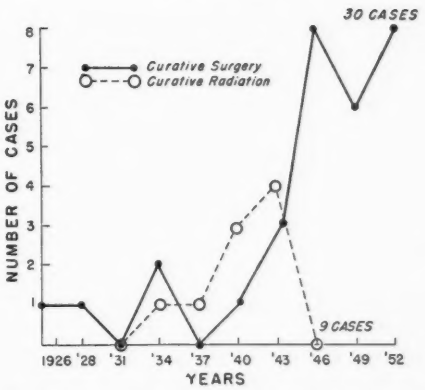

Fig. 6. Incidence of cases treated by curative surgery or by curative radiation.

treated in 1934. In the next 9 years, patients were treated by either method, a slight majority receiving radiation. None were treated at this hospital by a combination of the two methods. Since 1943, however, curative radiation has not been used in any instance. This change was apparently caused by the first reports of 5 year survival in our patients following surgery, which began to appear at about that time, as well as similar reports from other clinics, notably that of Cattell from the Lahey Clinic published in 1943, and by the appearance at this time of late recurrences in patients who had been considered cured by radiation. Another factor that apparently influenced the discontinuance of radiation treatment was the severe pain and discomfort that patients treated by it were experiencing. In the patients treated by curative surgery since 1943 the chief change has been the tendency for abdominoperineal resection to supplant local excision and perineal proctectomy as the procedure of choice because of the wider removal of the lymph nodes which it affords. The resection should include wide removal of the perianal skin and excision of the coccyx, posterior vaginal wall, and other resectable tissues which may be involved. We have had no experience with combined surgical and radiation treatment. There were 2 postoperative deaths in the surgically treated patients, both following abdominoperineal resection, an operative mortality of 6.5 per cent.

TABLE I.—SQUAMOUS CELL CARCINOMA OF THE ANUS IN 49 PATIENTS FROM 1916 TO 1952 INCLUSIVE

	1916–1947 (available for 5-yr. analysis)	1948–1952	Total
Curative resection	18*	8*	26
Curative local excision	3	1	4
Curative local excision + radium (elsewhere)	1	—	1
Radium needles (curative)	5	—	5
Radium needles + x-ray (curative)	4	—	4
Palliative radiation	5	1	6
No treatment	3	2	5
Total	39*	12*	51

*One patient had resection for recurrent cancer following radiation.

Thirty-eight patients with carcinoma of the anus were admitted to the Presbyterian Hospital from 1916 to 1947 inclusive and were available for 5 year follow-up analysis (Table II). None of these patients had had primary treatment elsewhere. Of these, 21 were treated by surgery alone. All had some type of curative excision done with the expectation of possible cure. Thirteen patients were treated by abdominoperineal resection, 5 by perineal proctectomy and colostomy, and 3 by local excision. Another patient underwent local excision followed by radiation in another hospital. Eight patients were treated by radiation alone with hope of possible cure, 4 by radium needles alone and 4 by radium needles and roentgen rays. In 4 of these patients colostomies were also done. In 5 patients the disease was so far advanced that only palliative radiation could be given. Two patients refused treatment and in 1 none was advised. Microscopic proof of the diagnosis was obtained in every case. Fourteen patients were alive 5 years after treatment, giving an absolute 5 year survival rate of 36.8 per cent. This included 12 of the 21 surgically treated patients and 2 of the 8 patients treated by curative radiation. There were 2 patients who were alive 5 years after treatment but who still had persistent cancer, giving an absolute 5 year clinical cure rate of 31.6 per cent. One is alive 63 months after abdominoperineal resection and the other developed recurrent cancer 16 years after treatment with radium needles and underwent an abdominoperineal resection 5 months ago. The recurrent disease appeared in the rectum 6 centimeters above the site of the original lesion and probably represents a delayed recurrence from a metastatic node. In comparison with these results, the absolute 5 year survival and cure rates for 777 patients with carcinoma of the rectum treated at this hospital from 1916 to 1945 inclusive were 25.6 and 24.2 per cent respectively (9). The better results in patients with squamous cell carcinoma of the anus came as a surprise. The series is of course a small one, however.

An analysis has also been made of the 5 year results in patients who received curative surgery or curative radiation treatment from 1916 to 1947, omitting those who received merely palliative treatment or none at all (Table III). There were 21 patients treated by surgery, 13 by abdominoperineal resection, 5 by perineal proctectomy and 3 by local excision. Eleven of these were alive 5 years after operation. One patient already mentioned is alive 63 months after abdominoperineal resection but has persistent cancer. It is of interest that 2 of the 3 patients treated by local excision were in the 5 year survival group. Both had local recurrences which were re-excised with apparent success. One died of other causes 6 years after the re-excision and the other has survived 4 years following it without evidence of recurrence. We do not recommend local excision, however, as it does not remove the lymphatic metastases. Seven of the 10 patients surviving 5 years without evidence of persistent cancer had tumors classed as large, and 3 had small lesions. There were only 8 patients treated by radiation in dosages sufficient for possible cure. Two of these were alive at 5 years. Both were treated by radium needle implants only. One was the patient already mentioned who had a local recurrence after 16 years and who underwent abdominoperineal resection of the rectum 5 months ago. The other patient is well without evidence of disease 10 years after radiation. Three of the patients given radiation therapy had local recurrences and were later treated by radical surgery. One of these had to have an abdominoperineal resection 10 months after

radium needles were implanted because of local recurrence and is now well 12½ years after operation. This patient was included among the 5 year survivals following surgery in Tables II and III. The group treated by radiation is, of course, too small to be of statistical significance. There was only 1 patient treated by surgery followed by radiation with hope of possible cure. This was a patient with a small tumor which was excised locally and 2 months later received prophylactic radium treatment at another hospital. This patient is well and without evidence of cancer nearly 7 years after treatment. The proportion of large and small tumors was about the same in the groups treated by surgery and radiation. The relative 5 year survival rate for patients treated by curative surgery was 52.4 per cent and the cure rate was 47.6 per cent. This can be compared to the relative 5 year survival and cure rates for 366 patients with carcinoma of the rectum treated by abdominoperineal resection at this hospital from 1916 to 1945 inclusive which were 46.4 and 43.4 per cent (9).

The degree and duration of pain accompanying radiation treatment from local irritation and necrosis and the effect of radiation on the function of the anal sphincter were also studied (Table IV). In 9 of 12 patients the pain was severe, in 2 moderate, and in 1 patient it was only slight. Its average duration was approximately 9 months. Its severity can be judged from the fact that 1 patient committed suicide because of it, another threatened suicide, and 2 patients had to undergo cordotomy to obtain relief from it. In 3 patients colostomies were done after radiation treatment to relieve the pain of defecation. In only 1 patient was a colostomy performed before radiation. Those with colostomies seemed to be definitely more comfortable. Radionecrosis and fibrosis of the anal tissues with resulting stricture and incontinence of varying degree occurred frequently. Only 1 patient had relatively normal sphincter function following radiation. It is probable that more modern techniques of radiation therapy such as the use of high voltage roentgen rays will prove less painful and cause less fibrosis of the anal sphincter than radium needle implantation.

TABLE II.—SQUAMOUS CELL CARCINOMA OF ANUS IN ALL PRIMARY HOSPITAL ADMISSIONS, 1916 TO 1947 INCLUSIVE

	No. of cases	No. of 5 year survivals	No. of 5 year survivals without persistent cancer
Abdominoperineal resection	13	6	5
Perineal proctectomy	5	3	3
Local excision	3	2	2
Local excision and radium applicator elsewhere (curative)	1	1	1
Radium needles (curative)	4	2	1
Radium needles & x-ray (curative)	4	—	—
Palliative radiation	5	—	—
Refused treatment	2	—	—
No treatment advised	1	—	—
	38	14	12

Absolute 5 yr. survival rate $= \frac{14}{38} = 36.8$ per cent

Absolute 5 yr. clinical cure rate $= \frac{12}{38} = 31.6$ per cent

DISCUSSION

The results reported from other clinics as well as those in the present series are shown in Table V. They are not strictly comparable in many respects. As complete figures are not reported in some of the series the absolute survival and clinical cure rates, which should be based on all primary patients seen or admitted, cannot be given. The cases of radiation treatment especially represent a selected group, whose basis of selection varies in each clinic. The relative rates represent results in patients treated with expectation of possible cure. In the series of cases treated by radiation the distinction is not always made between curative and palliative cases. The rates do offer, however, some basis for comparison. The results following radiation reported by Roux-Berger and Ennuyer from the Curie Foundation, by O'Brien, Lombardo, and Oppenheim (15) from the Roswell Park Institute at Buffalo, and by Paterson, Tod, and Russell from the Holt Radium Institute of Manchester, England, are impressive and compare favorably with any type of treatment. There is considerable doubt, however, among radiologists, surgeons, and pathologists as to whether radiation can destroy cancer in metastatic

TABLE III.—RESULTS OF CURATIVE TREATMENT IN 29 CASES, 1916 TO 1947, INCLUSIVE

Type of treatment	Surgery, 21 cases	Radiation, 8 cases
Abdominoperineal resection	13	
Perineal proctectomy	5	
Local excision	3	
Radium needles		4
Radium needles and x-ray		4
Operative deaths	2	
Death from intercurrent disease or unknown cause before 5 years	3	1
Death from cancer before 5 years	5	5
Alive with cancer persisting 5 years after therapy	1	1
Alive without cancer 5 years after therapy	10	1

Relative 5 yr. survival rate, 11/21, 52.4 per cent.
Relative 5 yr. clinical cure rate, 10/21, 47.6 per cent.

lymph nodes such as the perirectal and the mesocolic nodes which are not easily accessible. Perhaps the use of supervoltage radiotherapy equipment may accomplish this in the future. It seems probable that the good results reported with radiation therapy in the past have been chiefly in tumors without node metastases. On the other hand, surgery can be counted on to remove the perirectal and mesocolic node metastases in most instances as well as the primary tumor. This is certainly true in carcinoma of the rectum. In this series of carcinoma of the anus it can only be proved in 1 case, although it probably occurred in others. Of the 18 patients treated by either curative abdominoperineal or perineal resection from 1916 to 1947 inclusive, 8 were alive without evidence of recurrence 5 years after operation. Of these 8 patients, only 1 was found to have lymph node metastases in the excised specimen. This patient had 4 node metastases in 5 perirectal nodes examined and is alive and well 19 years after operation. In the specimens removed from the other 7 five year survivors no metastases were reported, but in 2 of the specimens no nodes were sectioned and in 2 others only 1 was examined. Obviously the examination was inadequate and of little value in these cases and did not rule out the presence of metastases.

O'Brien now believes that lesions which are annular and have invaded the sphincter muscles but are still operable should be treated by abdominoperineal or perineal resection instead of by radiation alone. He treats small tumors, 1 to 1.5 centimeters in diameter, by roentgen radiation and local excision of the lesion if the sphincter muscles are not invaded and there is no evidence of inguinal metastases. Similar lesions with enlarged inguinal nodes are treated by roentgen radiation and subsequent local excision followed by groin dissection. Other surgeons and radiologists as well as O'Brien also advise the use of radiation on small lesions which are more accessible and are less apt to have node metastases. Our objection to such a plan is that the small size of a tumor is no guarantee that it has not metastasized. In fact, we have had 4 small tumors, all about 3 by 3 centimeters in diameter or less which proved to have 6, 5, 4, and 1 metastases each, respectively. The only tumor which one can feel confident has not metastasized is the intramucosal lesion and we have only had 1 of these. For the same reason we are opposed to local excision even for small lesions and prefer a more radical surgical procedure. Binkley (2) has used a combination of radiation and surgery depending largely on the location and size of the tumor. He uses high voltage roentgen-ray therapy followed by either perineal or abdominoperineal resection. For tumors lying below the mucocutaneous line which were not included in our series he uses radiation therapy alone or radiation therapy followed by wide local excision. McQuarrie and Buie (13) have reported a series from the Mayo Clinic in which radical surgery was the treatment of choice with postoperative radiation given also in 76 per cent of the surgically treated cases. Radiation was used alone chiefly in patients considered inoperable.

There seems to be general agreement among surgeons and radiologists that inguinal node metastases should be treated by surgery. Radiation therapy has not proved curative. Whether these nodes should be removed routinely as a prophylactic measure is still an undecided question which cannot be determined until more information is available. Whether removal of metastatic nodes by inguinal dissection can be a curative procedure has not been determined as far as we know although

TABLE IV.—RESULTS OF RADIATION TREATMENT IN 12 CASES FROM 1919 TO 1952

Patient	Year	Treatment	Method	Colostomy	Pain	Result
W.O.	1923	Palliative	Ra applicator	o	Severe	Recurrence; untraced after 8 mos.
J.G.	1933	Palliative	X-ray	o	Severe	Anal stricture; died of cancer at 12 mos.
J.G.	1934	Curative	Ra needles + x-ray	o	Severe	Threatened suicide; died of cancer at 8 mos.
P.A.	1936	Curative	Ra needles	o	Severe	Some stricture; local recurrence after 16 years. Abdominoperineal resection 10-28-52
E.L.	1938	Curative	Ra needles + x-ray	o	Severe	Suicide because of pain at 13 mos.
M.B.	1939	Curative	Ra needles + x-ray	+	Severe	Stricture and obstruction; colostomy 14 mos. later with relief; died of cancer at 4¼ yr.
F.C.	1939	Curative	Ra needles + x-ray	o	Severe	Cordotomy for intractable rectal pain at 8 mos.; died of cancer at 38 mos.
V.B.	1941	Palliative	X-ray + Ra applicator	o	Moderate	Died of cancer at 17 mos.
G.L.	1943	Curative	Ra needles	+	Severe	Colostomy for pain after 5 mos.; cordotomy for rectal pain 1 mo. later; died 19 days post op. of pneumonia
A.L.	1943	Curative	Ra needles	+	Severe	Colostomy for pain at 4 mos.; without much relief; abdominoperineal resection at another hospital 1944; untraced
R.B.	1943	Curative	Ra needles	+	Slight	Colostomy before radiation treatment; alive without disease at 9⅝ yr. Closure of colostomy not possible because of incontinent anus
S.C.	1943	Curative	Ra needles	o	Moderate	Fair sphincter function; local recurrence after 10 mos.; abdominoperineal resection 1944. Alive without disease at 12½ yr.

TABLE V.—RESULTS REPORTED FROM OTHER CLINICS AND PRESENT SERIES

	Year	Treatment	No.	5 year survivals	
				No.	Per cent
Sweet Palmer Memorial and Mass. Gen. Hospitals	1947	Surgery or radiation (all cases seen)	77	13*	16.8 Absolute clinical cure rate
		Curative surgery abdominoperineal and perineal proctectomy	48	12*	25.0 Relative clinical cure rate
Roux-Berger Curie Foundation, Paris	1948	Radiation	51	18*	35.3 Clinical cure rate
O'Brien Roswell Park Mem. Inst., Buffalo, N.Y.	1950	Radiation (all cases seen)	47	14*	29.5 Clinical cure rate
		(all cases treated)	45	14*	31.1 Clinical cure rate
Paterson Holt Radium Institute Manchester, England	1950	Radiation (all cases seen)	30	10	33.3 Survival rate
		(all cases treated)	19	10	52.6 Survival rate
McQuarrie and Buie Mayo Clinic	1950	Surgery and/or radiation	99	26	26.3 Absolute survival rate
		Curative surgery and radiation	47**	19	40.3 Relative survival rate
Binkley Memorial Hospital, N.Y.	1950	Surgery and radiation (all primary cases seen)	83	27	32.3 Absolute survival rate
		Curative surgery and radiation	65	27	41.5 Relative survival rate
Present series	1953	Surgery or radiation (all primary cases admitted)	38	14	36.8 Absolute survival rate
		(all primary cases admitted)	38	12*	31.6 Absolute clinical cure rate
		Curative surgery	21	11	52.4 Relative survival rate
		Curative surgery	21	10*	47.6 Relative clinical cure rate

*5 year survival without persistent disease.
**76 per cent of patients treated surgically received postoperative radiation.

Pack and others have shown that it can be in epithelioma of the lower extremity, vulva, and scrotum. Reports from other clinics on the survival of patients with inguinal node metastases are scanty. All of our patients with proved inguinal node metastases died of recurrence in spite of groin dissection. Keyes had 4 similar patients, all of whom died of cancer. Until we have further knowledge it would seem logical to do radical groin dissection if the glands are enlarged or suspicious, and a routine prophylactic dissection when the primary tumor is large and extensive.

We believe that surgery, preferably by abdominoperineal resection, is the treatment of choice for carcinomas of the anus even for the small lesions. The upward lymphatic route to the perirectal and mesocolic nodes which is probably the most important can be removed by radical surgery. Radiation cannot be counted on to destroy lymph node metastases which may occur even in the smallest lesion. Radiation has in the past proved a very painful form of treatment, may have to be accompanied by colostomy, and frequently damages the sphincter with resulting stricture or incontinence. As we have already stated we have no experience with combined surgical and radiation treatment. With the more radical removal of the local and lymphatic spread of the tumor and the declining operative mortality the future results of squamous cell carcinoma of the anus following surgery should show continued improvement.

SUMMARY AND CONCLUSIONS

1. A series of 49 patients with squamous cell carcinoma of the anus, admitted to the hospital from 1916 to 1952 inclusive, has been presented. Five year follow-up results were obtained in 38 patients.

2. An early biopsy should be taken on all anal lesions to make sure that a carcinoma has not been overlooked.

3. Evidence of blood-borne metastasis was extremely rare in this series. It was found in only 2 patients, both of whom had liver metastases. It appeared to be less frequent than in a comparable series with rectal carcinoma.

4. Metastasis upward to the perirectal and mesocolic nodes along the superior hemorrhoidal vessels occurred in 7 of 25 specimens removed by abdominoperineal or perineal resection, an incidence of 28 per cent. Metastasis to the inguinal nodes was infrequent, occurring in only 4 patients and only late in the course of the disease.

5. It would appear from this series that upward spread to the perirectal and mesocolic nodes and lateral spread to the pelvic nodes may be as important as spread to the inguinal nodes, if not more so. More accurate studies of lymphatic metastases in these cases are urgently needed.

6. Before 1943 patients treated at this hospital with expectation of possible cure were treated either by surgery or radiation. Since 1943 they have been treated by surgery alone. Since then radiation has been used only as a palliative measure.

7. There were 38 patients admitted from 1916 to 1947 inclusive available for 5 year follow-up analysis. Fourteen patients were alive 5 years after treatment, giving an absolute 5 year survival rate of 36.8 per cent. Twelve patients were alive 5 years after treatment without evidence of persistent cancer, giving an absolute clinical cure rate of 31.6 per cent. Both rates compare favorably with those reported from this hospital for carcinoma of the rectum.

8. There were 29 patients treated with the expectation of possible cure between 1916 and 1947 inclusive. Twenty-one were treated by surgery and 8 by radiation. Eleven of the patients treated by surgery and 2 of those treated by radiation were alive 5 years after treatment. The relative 5 year survival and clinical cure rates for the surgically treated patients were 52.4 and 47.6 per cent respectively. Both the relative survival and cure rates compare favorably with those previously reported from this hospital for carcinoma of the rectum.

9. Radiation treatment was accompanied by severe and prolonged pain and resulted in partial anal stricture and incontinence in most of the patients on whom it was used.

10. Since it is questionable whether radiation can destroy cancer in nodes such as the perirectal and mesocolic it is believed that radical surgery by means of abdominoperineal resection offers the best chance for cure. As

local excision does not remove the regional lymph nodes, it is not recommended even in very small tumors which often have lymph node metastases. Radical surgery can be expected to improve the absolute and relative survival and cure rates still further in the future.

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AUREOMYCIN THERAPY OF CHRONIC PROSTATITIS

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THERE have been many favorable reports of aureomycin therapy of chronic urinary tract infections. Almost all of the cases reported have been those in which there were long-standing infections associated with urinary obstruction. Few of the studies included any patients with chronic prostatitis who had no other genitourinary diseases. Excellent results have been obtained with the prophylactic use of aureomycin following prostatectomy, but there have been only a few patients in whom aureomycin treatment of chronic prostatitis has been evaluated. It was therefore decided, because of the prevalence of chronic prostatitis, to study patients who had the disease, not associated with other urinary tract lesions, in an attempt to evaluate the results of antibiotic treatment. Aureomycin was selected for use in this study because it is effective against most of the species of bacteria found in urinary infections. High concentrations of aureomycin have been reported to occur in the urine following oral ingestion of small doses, and it was believed, therefore, that its use would afford a means of ascertaining the effect, if any, of high urinary concentrations of an antibiotic on an infection within the prostate gland.

MATERIALS AND METHODS

The studies reported upon herein were carried out on 20 patients with prostatitis who were treated at the University Hospitals of Cleveland and the Cleveland State Hospital. Patients having postprostatectomy infections or prostatitis associated with other genitourinary disease were not included in this study.

The patients were divided into three groups according to the dose of aureomycin administered to each. One group of 10 patients received 250 milligrams twice daily for 1 month, one group of 5 patients received 500 milligrams twice daily for 3 weeks, and the other group of 5 patients received 1 gram twice daily for 3 weeks. The drug was given orally to all patients. All other antibacterial therapy was stopped prior to the administration of aureomycin. Each patient had received previous treatment with one or more antibiotic or chemotherapeutic agents.

Positive prostatic and/or urine cultures were obtained in all patients before they were included in this study. Urine and prostatic secretion, secured by massage, were both taken aseptically for culture at each visit of 10 of the patients. In each of those 10 patients, massage of the prostate gland was performed weekly for 5 to 7 weeks. After treatment was begun, cultures were made weekly. In every case, following cessation of therapy, 3 to 4 specimens were cultured over a period of 2 to 3 months. All specimens were centrifuged and the sediments used for culturing. Each sample thus obtained was streaked on Endo and blood agar media and then incubated; one blood agar plate was placed under anaerobic conditions. All plates were examined after overnight incubation and organisms were identified.

Species of organisms isolated in pure cultures were tested in vitro for sensitivity to aureomycin by a serial tube dilution method (2). The highest concentration of aureomycin used in these determinations was 128 micrograms per milliliter; serial two-fold dilutions in thioglycollate broth were made to the lowest concentration of 0.5 microgram per milliliter. The aureomycin used for testing was inoculated in 0.5 milliliter quantities with 0.5 milliliter of a 10^{-3} dilution of an 18 hour broth culture of the organism to be tested. The tubes were examined after overnight incubation; complete inhibition of growth was selected as the end-point.

Urine was obtained for assay of the aureomycin content at varying intervals following

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ingestion of a dose of the antibiotic. In 4 patients, prostatic secretion, urine, and blood were obtained for assay 6 hours after a dose of 1 gram of aureomycin. The assay method, similar to that described by Herrell and Heilman, is one in which there is serial dilution in thioglycollate broth of the initial sample placed in the first tube. After dilution, 0.5 milliliter quantities remaining in each tube are inoculated with 0.5 milliliter of a 10^{-3} dilution of an 18 hour broth culture of Bacillus cereus. The tubes were examined after overnight incubation. A standard using aureomycin was freshly prepared every time samples were assayed. After determination of the end-point of the standard, the concentration of aureomycin in the sample was calculated.

RESULTS

Permanent sterilization of the urine was achieved in only 1 patient in this series. That patient received 250 milligrams of aureomycin twice daily and prostatic massage weekly for 4 weeks. Staphylococcus albus and beta hemolytic streptocci were isolated from the pretreatment urine and prostatic fluid. Cultures became sterile 3 weeks after the institution of treatment and repeated follow-up cultures continued to be sterile. Although sterilization was not effected in any other patient, eradication of some of the infecting organisms was achieved during the course of therapy. The organisms that persisted during and after each of the regimens of therapy are shown in Tables I to III. It is seen that there was elimination of 7 of the 18 infecting organisms in the 10 patients who received 500 milligrams of aureomycin daily. There was eradication of 3 of the 8 infecting organisms in the 5 patients who received 1 gram of aureomycin daily, and elimination of 3 of the 9 infecting organisms in the 5 patients who received 2 grams daily. It can be seen that the findings in each of the three groups of patients were essentially the same. The different doses of aureomycin and durations of treatment did not alter the results.

Nine of the 20 patients had pretreatment cultures in which there was only 1 infecting organism. There were 3 patients in whom more than 2 organisms were isolated from pretreatment cultures. Prostatic secretion and urine were obtained for culture at the same visit a total of 55 times. In 2 instances, the prostatic culture showed growth when the urine culture was sterile, and in 4 instances the urine culture showed the presence of organisms that were not demonstrated in the prostatic culture. Bacteriologic findings were the same in those patients who had prostatic massage as in those who did not.

Symptomatic improvement and significant diminution of pyuria and prostatorrhea occurred in all patients within 4 to 5 days after treatment was begun, despite the fact that a bacteriologic cure was achieved in only 1 patient. However, the clinical signs and symp-

TABLE I.—DISTRIBUTION OF MICRO-ORGANISMS BEFORE, DURING, AND AFTER THERAPY WITH 500 MILLIGRAMS OF AUREOMYCIN DAILY

Organism	No. of patients		
	Isolated before therapy	Persisted during and after therapy	Appeared during or after therapy
Staphylococcus albus	7	5	3
Alpha hemolytic streptococci	2	1	1
Beta hemolytic streptococci	1	0	1
Nonhemolytic streptococci	0	0	1
Proteus	1	1	4
Escherichia coli	3	1	1
Aerobacter aerogenes	3	2	1
Diphtheroids	1	0	0
Yeasts	0	0	0

TABLE II.—DISTRIBUTION OF MICRO-ORGANISMS BEFORE, DURING, AND AFTER THERAPY WITH 1 GRAM AUREOMYCIN DAILY

Organism	No. of patients		
	Isolated before therapy	Persisted during and after therapy	Appeared during or after therapy
Staphylococcus albus	4	4	1
Alpha hemolytic streptococci	1	0	0
Proteus	1	1	3
Escherichia coli	1	0	0
Paracolon	1	0	1
Alcaligenes faecalis	1	1	0
Yeasts	0	0	3

TABLE III.—DISTRIBUTION OF MICRO-ORGANISMS BEFORE, DURING, AND AFTER THERAPY WITH 2 GRAMS AUREOMYCIN DAILY

Organism	No. of patients		
	Isolated before therapy	Persisted during and after therapy	Appeared during or after therapy
Staphylococcus albus	4	3	1
Nonhemolytic streptococci	0	0	1
Proteus	1	1	3
Pseudomonas aeruginosa	1	1	0
Escherichia coli	1	0	0
Aerobacter aerogenes	1	0	0
Paracolon	0	0	1
Alcaligenes faecalis	0	0	1
Yeasts	0	0	1

toms returned at varying intervals after the cessation of therapy in all patients in whom infection persisted. The 1 patient whose urine was sterilized continued to be free of symptoms.

The in vitro sensitivities to aureomycin of 50 of the organisms isolated from the urine of the patients in this study are shown in Table IV. With the exception of yeasts, almost all of the organisms that appeared during treatment were tested. It can be seen that only the proteus organisms consistently required high concentrations in vitro for inhibition. The majority of the other organisms were inhibited by 20 micrograms per milliliter or less. There was no difference between the in vitro sensitivity values of the group of organisms that appeared after therapy was begun and the group of organisms that were isolated prior to therapy.

Assay of the aureomycin concentration in the urine was performed in 16 patients at varying intervals after the institution of therapy and at different intervals after oral administration of a dose of the antibiotic. Urinary concentrations ranged from 2 micrograms per milliliter to 64 micrograms per milliliter after a dose of 250 milligrams of aureomycin, and from 8 micrograms per milliliter to 256 micrograms per milliliter following a dose of 500 milligrams or 1 gram. There was no "piling up" effect demonstrated; that is, the levels obtained after several days or weeks of therapy were no higher than those obtained after a single dose of the drug. However, the interval between the ingestion of a dose and the collection of a specimen for determination did influence the level. There was no appreciable excretion in the first 2 hours following administration of a dose. The highest concentrations were found to be present 6 to 8 hours after oral ingestion.

Assay of the aureomycin concentration in the prostatic fluid of 4 patients showed the levels to be practically the same as those in blood obtained at the same time as the prostatic fluid. The concentration of aureomycin in the blood of each of the 4 patients was 2 micrograms per milliliter. The concentration in the prostatic fluid was 1 microgram per milliliter in 1 patient, 1.25 microgram per milliliter in another, and 2 micrograms per milliliter in each of the 2 other patients. Levels in urine samples obtained concomitantly were 64 micrograms per milliliter, 64 micrograms per milliliter, 16 micrograms per milliliter, and 128 micrograms per milliliter, respectively.

Administration of the doses of aureomycin employed in this study was associated with minimal untoward reactions. One patient who received 1 gram twice daily developed nausea on the eleventh day of treatment and the drug was discontinued. There were no other side effects encountered.

DISCUSSION

The results of this study demonstrate that aureomycin is ineffective in the treatment of chronic prostatitis. The different doses of aureomycin employed did not affect the results of therapy. There was eradication of 13 of the 35 infecting organisms that were isolated from pretreatment cultures. On the other hand, there were 28 organisms not cultured before therapy was begun that appeared after treatment was instituted. Ten of those 28 organisms were proteus and 4 were yeasts. This finding of the appearance of proteus and yeasts after the onset of treatment has been reported by others. Excluding the 14 instances in which those 2 species appeared after the institution of treatment, almost the

TABLE IV.—IN VITRO SENSITIVITY TO AUREOMYCIN OF BACTERIA ISOLATED FROM THE URINARY TRACT

Organism	No. cultures tested	No. of strains inhibited by less than 5μg./ml.	No. of strains inhibited by 5–20μg./ml.	No. of strains inhibited by 20–60μg./ml.	No. of strains inhibited by 60–125μg./ml.	No. of strains inhibited by 125μg./ml. or more
Staphylococcus albus	20	2	5	11	1	1
Nonhemolytic streptococci	2	2				
Escherichia coli	5	3	2			
Aerobacter aerogenes	4	2	1	1		
Proteus	13	1				12
Paracolon	3		2	1		
Alcaligenes faecalis	2		1	1		
Pseudomonas aeruginosa	1				1	

same number of organisms appeared during the course of therapy as were thought to have been eradicated. This change in the flora has been explained by others as being due to the appearance of secondary organisms following eradication of the initial infecting pathogenic organisms. However, it seems equally as plausible, since most of the organisms comprising the "secondary flora" were the same species as those comprising the initial culture, that this chronic disease may be characterized by a continually changing flora. If this were true, it would be difficult to be sure that the elimination of any organism were the result of the therapy administered. It may be that the treatment was not responsible for the disappearance or appearance of the organisms so categorized in Tables I to III, and the organisms that were classified as having persisted during therapy were those comprising the resident flora that is the "backbone" of the chronic infection. The facts that the results in each of the three groups of patients were essentially the same, and the organisms that appeared during therapy, with the exception of proteus and yeasts, were the same species and showed the same in vitro sensitivities as those that were cultured initially, lend further support to the possibility that the treatment had little effect on the existing bacterial flora in the prostate gland.

The finding that differences between prostatic and urine cultures are so infrequent indicates that separate cultures are not necessary for evaluation of the bacteriologic response to therapy.

It is shown that adequate concentrations of aureomycin occurred in the urine following administration of doses of the drug employed in this study. The urine levels obtained following ingestion of 1 gram were no higher than those obtained following ingestion of 500 milligrams, but both of these doses gave higher levels than were obtained following the administration of 250 milligrams. This is in keeping with the findings of others, who have shown that increasing the oral dose of aureomycin beyond an optimum amount does not produce proportionately higher blood levels because of the limiting factor of absorption of the antibiotic from the intestinal tract. Sirota and Saltzman have shown that the renal clearance of aureomycin in man is influenced solely by the glomerular filtration rate and the protein binding power of the plasma, and they concluded that the urinary concentration in any one individual is inversely proportional to the urine flow.

It is interesting that the urine aureomycin levels demonstrated by assay were significantly higher than the concentrations of aureomycin necessary for in vitro inhibition of the organisms. However, there is little reason to believe that the presence of high concentrations of an antibiotic in urine would have any effect on an infection in prostatic tissue, since effectiveness of the drug is dependent upon the concentration that can be attained in the gland itself. It can be seen from these results of prostatic fluid assays that there is no correlation between the excretion of an antibiotic in urine and the con-

centration in the prostate gland, which is the actual site of infection. As would be expected, the concentration in prostatic secretion is almost identical with the concentration in the blood stream. Examination of Table IV reveals that only 10 of the 50 organisms tested for in vitro sensitivity were inhibited by less than 5 micrograms per milliliter of aureomycin; of those 10 organisms, only 3 were inhibited by 2.5 micrograms per milliliter. Since the highest concentrations demonstrated in prostatic secretions were 2 micrograms per milliliter, one would expect little change in the bacterial flora of the prostate gland to be effected by aureomycin therapy.

In a previous study, the authors found that the treatment of chronic prostatitis with furadantin was ineffective (3). Although all of the antibiotics have not yet been evaluated in the treatment of this disease, it is believed on the basis of these clinical results correlated with assays and cultures of prostatic fluid, that antibiotics in the therapy of chronic prostatitis are of little permanent value.

SUMMARY

Twenty patients with chronic prostatitis not associated with any other genitourinary disease were treated with aureomycin. Permanent sterilization of the urine was achieved in only 1 patient. Different doses of the drug effected no change in the results. Thirty-seven per cent of the infecting organisms that were isolated from pretreatment cultures were thought to have been eradicated by the therapy. Many organisms appeared during or after the course of treatment and the possible meaning of this changing flora was discussed. Bacteriologic findings were not influenced by prostatic massage. Symptomatic improvement occurred in all patients within 4 to 5 days after the institution of treatment, but the clinical signs and symptoms returned in all in whom infection persisted. Adequate concentrations of aureomycin in the urine were demonstrated following administration of doses of the drug employed in this study but only small amounts of the antibiotic were detected in prostatic secretions. The importance of the concentration of antibiotic attained in prostatic tissue is discussed.

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CANCER OF THE UPPER THORACIC ESOPHAGUS

Combined Right Thoracoabdominal Approach

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MANY thoughtful surgeons believed that the problem of the management of esophageal cancer had been solved when Franz Torek in 1913 successfully resected the esophagus for malignant disease. His patient was a woman and she lived 9 years and then died free of cancer. The following two decades witnessed the gradual change from surgical optimism to abject pessimism.

In 1933, one of us (W.L.W.) examined the records of 506 cases of cancer of the esophagus at Memorial Center and expressed this opinion: "Only in the very unusual, early case should radical surgery be attempted, and a cured case of cancer of the esophagus will be something of a medical curiosity" (6).

A measure of hope returned during the next 20 years as we learned that surgical and biochemical advances would permit an increased range of operability; tend to reduce the operative mortality, and increase the possibility of an improved 5 year salvage rate (8, 9, 11).

MATERIAL

The first esophagectomy at Memorial Hospital was performed on March 12, 1940 and since that time 778 patients with cancer of the esophagus have been admitted to our hospital. Approximately 3 per cent of all patients coming to Memorial Cancer Center are found to have a malignant neoplasm located somewhere in the esophagus. The number of admissions varies from year to year between 36 and 59, and the total overall series available for study consists of 1,434 cases.

In 23 cases it was possible to do a cervical esophagectomy and plastic reconstruction. The thoracic esophagus was resected in 117 cases and of this group 45 procedures were of the right side, one stage, combined thoracoabdominal type. This represents 40 per cent of the total thoracic esophagectomies in the series.

In 10 of these patients anastomosis between the stomach and the esophagus was made above the clavicle employing a third incision (parallel to the anterior border of the sternomastoid muscle in the lower third of the right neck).

TECHNIQUE

Technically, satisfactory surgical procedures have been devised for the management of cancer of the cervical portion of the esophagus (10, 12, 13), and also for cancers located in the middle and lower thirds (2). When, however, cancer is located in the upper segment of the thoracic esophagus where it comes into intimate contact with the aortic arch and trachea, a particularly trying set of technical difficulties is encountered during surgical resection and anastomosis. In an attempt to lessen trauma, increase resectability, and facilitate wide surgical removal of malignant disease in the upper third of the esophagus, we have experimented with several different approaches. Unanimity of opinion does not obtain even among our own staff members, but nonetheless it is the consensus that the one stage, combined, right thoracoabdominal approach carried out by one or two operating teams has a number of definite advantages over the thoracoabdominal operation first recommended by Lewis or the one stage operation reported by Tanner.

Cancer at the level of the aortic arch presents a serious surgical problem with numerous technical difficulties. Therefore, the most meticulous preoperative preparation of the patient is needed in order to insure his safety. As a first step the surgeon in charge performs an esophagoscopy and a bronchoscopy in or-

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der to determine the immediate preoperative condition of the vocal cords, the level and extent of the esophageal cancer, the degree of fixation, and whether or not there is any suggestive evidence of mediastinal, bronchial, or tracheal invasion.

The medical consultant takes over here and supervises the restoration of electrolyte balance, corrects or improves the cardiovascular status, restores the blood factors to normal, and corrects, in so far as possible, the inanition and dehydration so commonly present in these patients. The internists charged with this responsibility find very few of our patients who cannot be operated upon because of age, debility, or heart disease, but many are denied surgery because of extension of disease into the lower cervical lymph nodes, the mediastinum, the trachea, bronchi, or other contiguous and vital structures. This, of course, is the problem of late diagnosis.

The next most important step in preparation for surgery is a consultation with the head of the Department of Anesthesiology. This meeting permits a calm preoperative study of the particular patient and his individual requirements leading to an unhurried decision regarding preoperative medication and proper anesthetic agents. For the average case, intratracheal gas, oxygen, and ether anesthesia is used, but in selected cases, sodium pentothal, oxygen, and curare have been employed.

After the patient has been anesthetized and carefully intubated, he is placed on the operating table in the left lateral recumbent position inclining backward at a 45 degree angle with the right arm suspended in a forward and elevated position, and a No. 15 intravenous needle inserted in the left ankle vein. The right thorax and upper abdomen are then prepared and a posterolateral incision beginning in the interscapular region is carried along the sixth rib to the costal margin. The sixth rib is removed subperiostally from the costal cartilage to within an inch of the transverse vertebral process. A 2 inch segment of the fifth rib proximal to the angle is similarly removed and the chest is opened and explored.

If removal of the cancer seems feasible, or if the surgeon elects to do a palliative by-pass operation, then a second team of operators extends the incision in a right paramedian fashion to the umbilicus for exposure of the stomach and exploration of the peritoneal cavity for metastases. Mobilization of the stomach is carried out in the customary fashion and usually is so complete that an anastomosis can easily be performed in the extreme apex of the thorax, or even in the lower neck. During the mobilization of the stomach the thoracic esophagus with its cancer is gently excised from the mediastinum and completely mobilized from the apex of thorax to the diaphragm.

The cardiac end of the esophagus is divided between clamps, and a portion of the cardia of the stomach may be sacrified if its blood supply appears to be in any way compromised. The stomach is then brought into the chest cavity, care being taken not to twist or rotate the mobilized stomach on its long axis, nor to bring more stomach into the chest than is actually needed. The anastomosis is then carried out between stomach and normal esophagus well proximal to palpable disease. In 10 patients the anastomosis between the stomach and the esophagus was carried out in the lower neck above the clavicle.

OPERATIVE MORTALITY

Cancer of the esophagus at the aortic level is admittedly a difficult disease to handle surgically, and the right sided approach is usually employed in the hope that a borderline setting may become resectable because of better exposure of the aorta and mediastinum. This, of course, leads to more aggressive surgery and adds to the operative risk and danger to the patient. In our series of 45 resected cases there were 11 postoperative deaths, or 24.4 per cent.

ADVANTAGES

The combined right thoracoabdominal approach for cancer of the upper thoracic esophagus we believe provides the following advantages:

1. It permits better cancer surgery because a more extensive resection of potentially involved esophagus can be done with a minimum of technical difficulty.

2. It affords an increased range of resectability in cases in which disease is closely ad-

herent to bronchus and arch of aorta because the dissection in this region can be carried out under direct vision. The shock-producing blunt dissection behind the arch of the aorta, which is so often necessary when the operation is performed from the left side is largely avoided.

3. There is less danger of accidentally entering the opposite pleural cavity, and when a segment of opposite pleura must be resected because of extension of disease it can be done under direct vision.

4. The exposure obtained by this procedure readily permits gastroesophageal anastomosis at, and occasionally above, the superior thoracic aperture. Adequate exposure is obtained without the necessity of resecting numerous ribs or transecting the diaphragm. Added exposure, if necessary, may be obtained by transecting the costochondral junction of the sixth, seventh, and eighth ribs.

5. At the completion of the operation, the stomach lies in the mediastinum in a more satisfactory anatomic position. There is practically no tension, and the blood supply is excellent.

6. If a resection cannot be accomplished because of the extent of disease, one is still permitted to do a palliative by-pass operation, which, to our way of thinking, provides more temporary relief than does a Janeway gastrostomy (7).

7. The operating time may be shortened by employing two surgical teams who work simultaneously, one in the abdomen and the other in the chest.

8. If the patient is properly placed on the operating table he need not be turned or moved during the operation. As Burstein and co-workers have indicated, turning the patient during this type of surgery, we think, is definitely hazardous.

9. Postoperatively, it seems that the patients develop less gastric atony, pylorospasm, or other vagotomy effects.

10. The dangerous delay of a two stage procedure for cancer is avoided.

DISADVANTAGES

The disadvantages of the procedure are as follows:

1. Added anatomic dangers at the diaphragmatic level because of the proximity of the inferior vena cava, pleura of left chest cavity, and hepatic vein which may be injured when working through the esophageal hiatus.

2. The degree of abdominal exposure may be lessened by the adverse position of an enlarged liver.

3. Simultaneous surgery in the thorax and chest increases the likelihood of shock. Gentle handling of tissues is essential.

4. Two operative wounds add to the theoretic danger of wound sepsis.

5. The upper abdominal wound does add to the patient's postoperative discomfort and may interfere with adequate pulmonary ventilation.

END RESULTS

Of the 45 patients who had surgically successful right thoracic esophagectomy, 33 are now dead, 11 after operation and 22 of disease, 8 patients are living, the longest survival is 35 months. Two patients were alive for 18 months, 2 for 9 months, and 3 for less than 6 months. Four patients have been lost to follow-up and are presumed to be dead.

The prognosis for patients with cancer of the esophagus located at the aortic arch level is notoriously bad, and yet some measure of improvement may result from an increased resectability rate when the disease is approached from this side of the thorax.

SUMMARY

Cancers located in that portion of the esophagus between the upper thoracic inlet and the aortic arch have proved to be technically difficult surgical problems. These may be satisfactorily resected by using a combined, right thoracoabdominal approach.

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THE EFFECT OF SURGERY ON DOGS FOLLOWING WHOLE BODY X-IRRADIATION

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IN THE atomic explosions at Hiroshima and Nagasaki less than 15 per cent of the casualties resulted from ionizing radiation. A much greater number of patients received varying amounts of ionizing radiation in addition to burns and trauma. The effect of ionizing radiation on the clinical course of patients with burns and traumatic injuries was not well evaluated because of the confusion which prevailed immediately following the atomic bombings. Such data would be of great value in the event of future casualties resulting from atomic explosions.

Of particular interest to us was the zone an intermediate distance from hypocenter where many mixed casualties resulting from a combination of ionizing radiation and trauma were found. Included were many individuals who were indoors during the atomic explosion or who for some other reason were protected from the thermal effects of the atomic detonation. The distance and extent of this intermediate zone from the hypocenter would depend upon the magnitude of the nuclear energy dissipated.

This investigation was designed to determine whether or not surgical trauma superimposed upon whole body x-irradiation markedly altered the mortality. Dogs were chosen as the experimental animal since they lend themselves well to both surgery and whole body irradiation. An amount of irradiation was given which produced some mortality in itself but was distinctly less than a 100 per cent lethal dose. This would enable us to evaluate the effect of surgery in an animal receiving an appreciable amount of whole body x-irradiation.

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METHOD

Male mongrel dogs having a mean body weight of 8.6 kilograms were paired on the basis of estimated age, body weight, and white blood cell count. Both dogs in a pair were irradiated simultaneously and then one was randomly selected for surgery. A total of 18 pairs of dogs was studied. Ten pairs received 200 roentgens and 8 pairs received 300 roentgens of whole body irradiation. No antibiotics were administered since these are known to influence the mortality and survival time in injury from ionizing radiation as Koletsky and Miller and their associates have pointed out. The animals were irradiated without anesthesia in a circular cage 70 centimeters in diameter, 25 centimeters high, side and bottom of 75 per cent aluminum alloy, and top and dividing partition of lucite. Twelve circular holes 4 centimeters in diameter distributed along the circumference of the cage served as air vents. The physical factors of irradiation were as follows: 220 kilovolts; 15 milliamperes; mean target distance 148.5 centimeters; filters of 1 millimeter aluminum and ½ millimeter copper; half-value layer 1.35 millimeter copper; output in air 12.5 centimeters from the bottom of the cage and equidistant between the center and the periphery was 6.7 per minute.

Approximately 20 hours following whole body irradiation, surgery was performed under 25 milligrams per kilogram sodium pentobarbital anesthesia. The operative technique was as follows. The skin of the abdomen and lower thorax was shaved, scrubbed with phisohex, and painted with zephiran solution. The field was draped and an 8 centimeter right rectus incision was made. Bleeding was controlled with hemostats and No. 00000 braided silk ligatures. The cecum was identified and a 10 centimeter segment of ileum was resected approximately 15 centi-

TABLE I.—MORTALITY AND MEAN SURVIVAL TIME FOLLOWING WHOLE BODY IRRADIATION

Dosage r	Group	No. of dogs	No. of deaths	Per cent mortality	Mean survival time (days)
200	Control	10	3	30	16
200	Operated upon	10	2	20	37
300	Control	8	4	50	13
300	Operated upon	8	6	75	13

meters from the ileocecal valve. An open side-to-side anastomosis was performed using an inner continuous No. 00 intestinal chromic gut and an outer interrupted No. 0000 braided silk suture. The wound was closed in layers with Nos. 0000 and 00000 braided silk sutures. In all 10 of the 200 roentgen and in 3 of the 300 roentgen group, the skin was closed with a subcuticular suture of No. 0000 braided silk. In the remaining 5 dogs in the 300 roentgen group the skin was closed with No. 00000 interrupted silk suture. No dressing was applied.

Laboratory procedures consisted of the following: white blood cell count, red blood cell count, hemoglobin, total serum protein, and body weight. Two determinations of each were carried out prior to irradiation. White blood cell counts and body weight were recorded twice weekly for 3 weeks following irradiation and once weekly thereafter. Red blood cell count, hemoglobin, and total serum protein were performed weekly throughout the experiment. The dogs were carefully observed during the 60 day experimental period. Autopsies were performed on all dogs dying during this period.

TABLE II.—MEAN WHITE BLOOD CELL COUNTS PER MM.^{3} TIMES 10^3

Time in days	200 r Control		200 r Operated upon		300 r Control		300 r Operated upon	
	No.	WBC	No.	WBC	No.	WBC	No.	WBC
Control (2)	19	10.3	20	11.2	16	9.7	16	11.8
1–7	18	5.3	20	8.0	24	5.9	24	6.7
8–14	19	3.6	19	4.0	14	2.3	16	0.8
15–21	15	4.2	22	5.0	12	1.9	5	0.8
22–28	9	4.3	13	6.8	7	2.9	3	1.5
29–35	8	6.6	11	9.2	5	6.6	2	2.4
36–42	7	7.5	9	11.3	5	7.5	2	11.2
43–49	7	13.3	6	13.7	4	8.4	2	14.0
50–56	7	8.9	7	13.7	4	9.0	2	10.9
57–63	8	9.2	8	10.8	4	8.9	2	8.7

RESULTS

Mortality. Three of the 10 control dogs receiving 200 roentgens died, a mortality of 30 per cent (Table I). Only 2 of the 10 operative dogs receiving 200 roentgens died, a mortality of 20 per cent. Of the 8 pairs of dogs in the 300 roentgen group, 4 controls and 6 operative dogs died, a mortality of 50 and 75 per cent respectively. The overall mortality for the 18 pairs of dogs in the control and operative groups was 39 and 44 per cent respectively. It is evident that removal of a segment of ileum 20 hours postirradiation did not significantly alter the mortality in dogs receiving 200 or 300 roentgens of whole body irradiation.

Survival time. The survival times in the 300 roentgen groups were identical (Table I). In the 200 roentgen group too few dogs were involved to make any deductions of the effect of surgery on survival time. One dog in the 200 roentgen operative group died of a surgical complication on the 48th postradiation day.

Wound healing. In the ten 200 roentgen operative dogs the skin closures were all accomplished with subcuticular silk sutures and all healed per primam. In the 300 roentgen operative dogs 3 of the skin closures were of this type and all healed per primam. In the remaining five 300 roentgen operative dogs the skin was closed with interrupted silk sutures. In 3 of these dogs the wounds became infected. In 1 dog the wound healed by second intention while in the 2 remaining animals there were ulceration and infection at the time of death on the 13th and 15th postirradiation days.

White blood cell counts. In the 200 roentgen group decrease in white counts following whole body irradiation was more abrupt in the control than in the operative dogs during the first postirradiation week. The mean for the first 7 days was 5,300 and 8,000 for

the control and operative groups respectively (Table II). Thereafter, there was greater variability of the white counts in the operative dogs with a tendency for some white counts to be very high, thus increasing the mean. In the 300 roentgen group the mean white blood count during the first postirradiation week was only slightly higher for the dogs operated upon than for the control dogs, being 6,700 and 5,900 respectively. Seven pairs of dogs had white counts performed on the second postirradiation day (3 pairs in the 200 roentgen and 4 pairs in the 300 roentgen group). In all 7 control dogs the white counts were lower than the mean preirradiation counts while in all 7 operative dogs (first postoperative day) the white counts were increased above the mean preirradiation value (Table III). The mean white count for the control and operative dogs on the second postirradiation day was 6,300 and 16,800 respectively. There seems little doubt that this increase in white count was the direct result of surgical trauma.

Red blood cell counts. Following whole body irradiation the red cell counts decrease in all four groups of dogs (Table IV). There is little difference between the control and operative dogs in the 200 or 300 roentgen groups.

Hemoglobin. The postirradiation hemoglobin values follow the same trend as the red cell counts (Table V).

Body weight. There is only a slight decrease in body weight following 200 or 300 roentgens of whole body irradiation in both the control and operative groups (Table VI).

Total serum proteins. There is only a slight decrease in serum protein following whole body irradiation in both the control and operative groups (Table VII).

Pathological findings. Grossly, in the 200 roentgen operative group the small intestine appeared normal or showed only slight hyperemia at the time of surgery (20 hours postirradiation). In the 300 roentgen operative dogs there was slight to moderate hyperemia. In the 15 autopsies performed (6th to 48th postradiation day) the most common lesion was in the lung. The organ was usually dark pinkish-red, showed slight to marked loss of crepitance, sectioned with ease, the cross section exuding an abundant amount of pink fluid. The next most common lesion was petechiae of the kidney, heart, and gastrointestinal tract, most commonly found in dogs autopsied after the tenth postirradiation day.

TABLE III.—CONTROL AND SECOND POSTIRRADIATION DAY WHITE BLOOD COUNTS PER MM.^{3} TIMES 10^3

X-irradiation dosage r	No. of pairs	Irradiation only		Irradiation and operation	
		Mean control WBC	Second day WBC	Mean control WBC	Second day WBC
200	3	9.9	5.4	10.1	15.1
300	4	10.2	7.0	12.7	18.0

Microscopically, sections of ileum removed from dogs receiving 200 roentgens (20 hours postradiation) showed minimal irradiation effect in the form of nuclear pyknosis and rhexis, at the base of the crypts of Lieberkühn. In similar sections from the 300 roentgen group this change was moderate. In both the 200 and 300 roentgen groups there was moderate to marked cellular exudate at the base of the glands, submucosa, and to a lesser degree in the muscular coat. In all the dogs dying before the 30th postirradiation day the lungs showed a profound bacterial pneumonitis with varying amounts of edema, hemorrhage, and necrosis. Two dogs dying on the 30th and 48th postirradiation day did

TABLE IV.—MEAN RED BLOOD CELL COUNTS PER MM.^{3} TIMES 10^6

Time in days	200 r Control		200 r Operative		300 r Control		300 r Operative	
	No.	RBC	No.	RBC	No.	RBC	No.	RBC
Control (2)	19	5.3	20	5.4	16	5.3	16	5.3
1–7	6	4.7	9	5.0	19	4.5	17	4.3
8–14	11	4.9	10	4.4	6	4.1	8	3.6
15–21	8	4.7	14	3.8	4	3.7	4	2.9
22–28	7	5.1	13	3.8	5	3.6	1	2.0
29–35	8	4.3	11	4.0	5	3.6	2	2.8
36–42	7	4.1	9	4.0	5	4.3	2	3.7
43–49	7	4.2	8	4.4	4	4.0	2	3.8
50–56	7	4.4	7	4.5	4	4.5	2	3.9
57–63	8	4.4	8	4.7	3	4.2	2	4.0

TABLE V.—MEAN HEMOGLOBIN IN GRAMS PER 100 MILLILITERS OF WHOLE BLOOD

Time in days	200 r Control		200 r Operative		300 r Control		300 r Operative	
	No.	Hgb.	No.	Hgb.	No.	Hgb.	No.	Hgb.
Control (2)	19	14.3	20	14.0	14	13.8	16	13.5
1–7	8	13.3	10	13.1	17	12.8	15	13.1
8–14	12	12.9	10	11.8	9	11.9	11	10.6
15–21	10	12.5	16	11.5	5	9.8	3	8.5
22–28	9	12.4	13	11.7	5	11.6	1	7.4
29–35	8	12.8	11	12.5	5	9.8	2	8.1
36–42	7	13.1	9	12.5	5	11.4	2	9.7
43–49	7	12.7	8	13.5	4	12.2	2	11.2
50–56	7	13.4	7	13.5	4	12.2	2	12.6
57–63	8	14.3	8	13.4	4	12.4	2	12.7

not show this lesion. In the 15 autopsies performed, 6 of the dogs showed petechiae while in 3 additional animals there was focal hemorrhage. The kidney was the most common site being involved in all 9 cases in which hemorrhage was found. The heart was the next most common site being involved in 5 cases, while the gastrointestinal tract and spleen were involved in 2 cases each. In the spleen there was depletion of both the red and white pulp with the red pulp showing the greater depletion. There was marked depletion in the bone marrow of animals dying in the early period following irradiation. Those dying later showed a variable degree of repair.

TABLE VI.—MEAN BODY WEIGHT IN KILOGRAMS

Time in days	200 r Control		200 r Operative		300 r Control		300 r Operative	
	No.	Wt.	No.	Wt.	No.	Wt.	No.	Wt.
Control (2)	15	9.5	15	9.0	11	7.3	12	8.4
1–7	18	9.0	21	8.7	22	7.7	23	7.9
8–14	19	8.9	19	8.8	14	7.8	16	7.2
15–21	14	9.2	22	8.8	12	7.9	5	5.8
22–28	9	9.6	13	9.0	7	8.4	3	5.6
29–35	8	9.5	11	9.4	5	8.0	2	6.3
36–42	7	9.6	9	9.3	5	8.6	2	6.8
43–49	7	9.7	8	9.5	4	8.8	2	6.8
50–56	7	9.7	7	9.4	4	8.6	2	6.8
57–63	8	10.0	7	10.8	4	8.8	2	6.8

Clinical data. During the first 24 to 48 hours following irradiation the dogs appeared normal. In some instances there was mild or moderate anorexia beginning on the third or fourth postirradiation day. Two to 4 days prior to death there was usually anorexia or complete refusal of food which persisted until death. Terminally there was lacrimation, lethargy, fever, poor body turgor, and a dry crust on the nose. In some of the surviving dogs there was a period of anorexia for several days with recovery. The clinical course of the dogs operated upon was similar to that of the controls except for the operative period. The dogs were not fed on the day of operation, but were offered food on the first postoperative day. However, their food consumption at this time was less than that of the controls. By the second postoperative day (third postirradiation day) appetite, food consumption, and general clinical appearance of the two groups was similar.

DISCUSSION

The combined mortality (200 and 300 roentgen groups) for the 18 pairs of dogs was 7 and 8 in the control and operative groups respectively. This is a mortality of 39 per cent in the control and 44 per cent in the operative dogs. This difference is not significant. In this series an abdominal laparotomy and resection of a segment of ileum was well tolerated in dogs receiving 200 or 300 roentgens of whole body irradiation 20 hours prior to surgery. It seems probable that the results would not have been markedly different if surgery had been performed immediately following irradiation, or any time up to 20 hours following irradiation. However, one cannot conclude from these data what the results would be if surgery were delayed for a longer period of time following irradiation. It seems probable that the results would not be nearly as favorable for surgery if a major procedure were performed upon an animal already sick and having a markedly impaired body defense mechanism.

It is of interest that the white blood cell count responded to surgical trauma after 20 postirradiation hours. At a time when the white count is already decreased the re-

sponse is similar to what one might expect in a normal dog.

The case histories of 3 dogs are of interest and will be briefly discussed. One dog in the 200 roentgen operative group was mistakenly subjected to devocalization on the 20th postirradiation day. Following the procedure the dog bled profusely for about 1 hour. One liter of saline was administered to combat shock. The day following the procedure the dog developed a cough, showed clinical evidence of progressive dehydration, and pneumonia, and died on the 26th postirradiation day. At autopsy there was ulceration and necrosis at the operative site in the larynx. There was also a marked bacterial pneumonitis. Two days prior to devocalization the animal had been making a satisfactory clinical recovery and had a white count of 3,400 cells per cubic millimeter. Although it cannot be established that devocalization was the precipitating factor in the cause of death, the evidence is strongly suggestive.

A second dog in the 200 roentgen operative group died on the 48th postirradiation day and at autopsy had a gangrenous loop of small bowel caused by an adhesive band. In a 200 roentgen control dog there was spontaneous rupture of an interdigital cyst on the 20th postirradiation day. Although bleeding from this cause is usually minimal in the normal dog, this animal bled profusely. It can be assumed that this massive hemorrhage only hastened death and was probably not the immediate cause of death since 2 days prior to the hemorrhage the white count was only 400 cells per cubic millimeter. It is probable that the platelet count was also low at this time.

The problem of mixed injuries resulting from atomic explosion has not been studied exhaustively. Brooks and associates have studied the relation of burns to total body irradiation in dogs. They produced a standard deep second degree burn involving 20 per cent of the skin surface and studied the effect of 25 and 100 roentgens whole body irradiation. Twenty-five roentgens had no deleterious effect upon the mortality in dogs receiving a 20 per cent body surface burn. However, the animals receiving 100 roentgens in addition to a 20 per cent body surface burn had a mortality of 73 per cent compared with a mortality of only 12 per cent for the burn injury alone. One hundred roentgens alone gave no mortality in 10 dogs. When dogs with a 20 per cent burn plus 100 roentgens irradiation were treated with penicillin the mortality was decreased from 73 per cent in untreated dogs to 14 per cent in the treated animals.

TABLE VII.—MEAN TOTAL PROTEIN IN GRAMS PER 100 MILLILITERS OF SERUM

Time in days	200 r Control		200 r Operative		300 r Control		300 r Operative	
	No.	Gm.	No.	Gm.	No.	Gm.	No.	Gm.
Control (2)	18	6.1	20	6.2	16	5.9	15	6.0
1–7	5	5.5	6	5.8	11	5.8	13	5.6
8–14	10	5.5	12	5.4	8	5.5	9	5.2
15–21	8	5.9	10	5.5	6	5.8	4	5.5
22–28	8	5.7	11	6.1	6	5.6	1	6.2
29–35	6	5.8	7	6.0	5	5.4	2	5.8
36–42	7	5.9	9	5.9	5	6.1	2	5.1
43–49	7	6.0	8	6.0	4	6.2	2	5.1
50–56	7	6.1	7	6.0	4	5.7	2	5.7
57–63	8	6.1	7	6.0	4	5.8	2	5.7

Baxter and associates exposed young swine to 400 roentgens of whole body irradiation and observed a mortality of 20 per cent. When a group of animals were exposed to flash burns involving 10 to 15 per cent body surface there was no mortality. However, combining 400 roentgens of whole body irradiation and a 10 to 15 per cent body surface burn increased the mortality to 90 per cent. Parenteral streptomycin reduced the mortality of the last group to 20 per cent.

Both Brooks and Baxter and their associates observed that a combination of thermal injury and whole body irradiation resulted in an increased mortality over either thermal injury or whole body irradiation alone. However, in this investigation the combination of irradiation and surgical trauma performed under aseptic conditions did not significantly alter the mortality compared to irradiation alone. This difference can be easily explained by the marked difference between the bacterial contamination in burns and surgical wounds.

SUMMARY

Resection of a segment of ileum was well tolerated in dogs receiving 200 or 300 roentgens of whole body x-irradiation 20 hours prior to surgery. Mortality in 18 pairs of dogs was 39 per cent for animals receiving irradiation alone and 44 per cent for the group receiving irradiation and surgery. On the first postoperative day the white blood count of dogs operated upon was increased 41 per cent above the mean preirradiation count while in control dogs the white count during the same period was decreased 37 per cent. The surgical wounds healed remarkably well in the operative dogs. Wound infection did not occur in those dogs having skin closures of subcuticular suture. The most common pathologic finding in dogs dying following irradiation was a profound bacterial pneumonitis.

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THE USE OF ERYTHROMYCIN IN CERTAIN SURGICAL INFECTIONS

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FOLLOWING the introduction of penicillin, the problem of coccal infections, with few exceptions, appeared to be solved. Although penicillin still continues to be the drug of choice for coccal infections, it has among its limitations, the occurrence of infections with organisms resistant to this antibiotic. Staphylococcic infections are the most serious problem confronting the surgeon from this point of view. The staphylococcus is the only organism originally predominantly sensitive to penicillin which has shown a pattern of increasing resistance to this antibiotic. This is also occurring with respect to other antibiotics. A statistical study by one of us (2) revealed that there were twice as many staphylococcal strains resistant to penicillin among those which were "broad spectrum" antibiotic resistant than among those which were "broad spectrum" sensitive. It must be emphasized that penicillin resistance to staphylococci is of greater magnitude in hospital communities than in the community at large. Cross infections occur apparently not only from patient to patient but also through hospital personnel carriers of Staphylococcus aureus. Furthermore, failure of treatment at home is often a cause for hospital admission, and such failure may have as its basis antibiotic-resistant infection.

Beta hemolytic streptococcal infections have presented no real problems of antibiotic resistance and there is no evidence that they are going to do so. The other streptococcal infections, those due to alpha and nonhemolytic streptococci, particularly the enterococci, have been difficult to treat with penicillin. Many alpha hemolytic streptococci have been sensitive to penicillin and remain so. The enterococci, on the other hand, have been penicillin resistant from the beginning. This is also true to a certain extent for the newer antibiotics. For this reason combination therapy is commonly employed for alpha and nonhemolytic streptococcal infections, especially endocarditis.

Inadequate knowledge of the mechanisms by which resistant organisms emerge and, in some instances, perpetuate infection in patients has made it necessary that a continued search be made for new agents. One of these agents is erythromycin.

The discovery of erythromycin ("ilotycin," "erythrocin") was first announced by McGuire in 1952. It is elaborated by a soil actinomycete, Streptomyces erythreus. The purified antibiotic is basic and readily forms salts with acids. Its water solubility is 2 milligrams per milliliter. The drug is reasonably stable, but rapid decomposition occurs at *p*H 3 or less.

Erythromycin is active in vitro against most gram-positive cocci irrespective of whether they are sensitive or resistant to other antibiotics (except carbomycin). It is also active against the diphtheria bacilli, Actinomyces israeli, some pathogenic clostridia, and the gram-negative neisseria and hemophilus species. This agent also shows activity against a number of other microbes in vivo, including certain rickettsiae and the viruses of lymphogranuloma and mouse meningopneumonitis in chick embryos, and Endameba histolytica, Trichomonas vaginalis, Spirochaeta novyi, and oxyurids in mice. Little or no activity is exerted against the gram-negative enteric bacilli, Nocardia asteroides, the pathogenic mycobacteria, fungi, and small viruses. In general, erythromycin overlaps penicillin in its antimicrobial spectrum.

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Erythromycin can be bacteriostatic or bactericidal depending upon its concentration and the sensitivity of the organisms. The emergence of resistance has been reported in vitro by incubation of staphylococci and streptococci in sublethal or graded concentrations of the drug and in vivo in erythromycin-treated patients. Three instances of the emergence of erythromycin-resistant staphylococci were observed in the presently reported series of 60 clinical cases. Cross-resistance between erythromycin and carbomycin, whose antimicrobial spectra are similar, has been demonstrated in vitro for micrococci and streptococci.

Erythromycin, originally available in capsules, is now mainly supplied in the form of 100 milligram enteric-coated tablets for oral administration. Preparations for intramuscular or intravenous administration are available at this time for clinical investigation. Kirby, Maple, and O'Leary found that higher serum concentrations were obtained when acid-resistant coated tablets rather than gelatin capsules were administered. Administration of 500 milligrams of the former type product every 6 hours to adults led to serum levels of 2 to 50 micrograms per milliliter. Once in the bloodstream, the drug diffuses into ascitic and pleural fluids and through the placenta in therapeutic concentrations. In patients with meningitis the level in the cerebrospinal fluid is from one-sixteenth to one-fourth of the serum concentration. Erythromycin is concentrated in the normal liver and excreted into the biliary tree in active form. The erythromycin level in the common duct bile of one of our patients with postcholecystectomy pericholangitis was 30 times that of the serum. The amounts of the drug recovered in the urine may vary considerably, but usually about 15 per cent of the administered dose can be accounted for. Therapeutic concentrations of erythromycin can be detected in the prostatic secretions of patients with genitourinary disease after the ingestion of a 500 milligram dose. Erythromycin is only partially absorbed from the gastrointestinal tract and the unabsorbed drug has a suppressive effect upon susceptible gram-positive fecal organisms. Its administration is accompanied by gastrointestinal distress in some patients. No other toxic phenomena have been reported.

At the time of this writing there are reports in the literature of 101 cases of infections treated with erythromycin given orally. Thirty-four of these patients had streptococcal infections, of which 28 cases were reported to have responded to erythromycin therapy. The drug was effective in 29 out of 34 cases of pneumococcal infections, mainly lobar pneumonia, and ineffective in 5 others. There were 9 reported staphylococcal infections; good results were obtained except in 2 cases of staphylococcal endocarditis. In both instances emergence of erythromycin-resistant organisms was noted. Results of treatment in 25 miscellaneous cases have also been published, including gonorrhea, nonspecific urethritis, diphtheria carriers, staphylococcal and streptococcal pharyngitis, staphylococcal endocarditis, osteomyelitis, carbuncle, and erysipelas. The successful use of erythromycin ointment in acute gram-positive coccal pyoderma in children has also been reported by Freeman and Scott. The present report presents experiences with the use of erythromycin therapy in certain surgical infections.

CLINICAL TRIAL OF ERYTHROMYCIN

Erythromycin therapy was evaluated in 60 adult patients with infections in the following categories: (1) those caused by staphylococci; (2) infections caused by streptococci or by combinations of streptococci and staphylococci; (3) genitourinary tract infections; and, (4) mixed infections due to gram-positive cocci and gram-negative bacilli.

With the exception of 1 closed infection and some of the genitourinary infections, cultures were made in all cases, and antibiotic sensitivity tests by the serial tube method were performed on the isolates. Gram-positive cocci were tested for sensitivity against penicillin, streptomycin, chlortetracycline, oxytetracycline, and chloramphenicol. Penicillin-resistant cocci were tested against erythromycin. Erythromycin was used in many instances only after other antibiotics were administered and found to be ineffective, and culture sensitivity tests revealed the causa-

tive organisms to be penicillin-resistant. All penicillin-resistant gram-positive cocci studied were found to be initially erythromycin-sensitive.

The usual dosage of erythromycin was 400 milligrams every 6 hours, either in capsule or tablet form. Total dosages varied from 4.8 to 96 grams. The shortest period of therapy was 4 days and the longest 42. Erythromycin concentrations were determined in over 50 different sera approximately 2 hours after its administration. It was found that in 82 per cent of the cases the blood serum level was in excess of 0.3 microgram per milliliter and in 64 per cent of the cases in excess of 1.2 micrograms per milliliter.

In evaluating clinical results of erythromycin therapy, the following criteria were employed: An excellent response was considered one in which there was complete or nearly complete resolution of the infection within 72 hours. A good response implied complete resolution in a longer period of time but shorter than the expected time of resolution of the infection on empiric or adjunctive therapy alone. An equivocal response was considered to be one in which it could not be determined whether resolution of the infection was due to antibiotic therapy or other cause. No response was one in which antibiotic therapy had no effect.

The overall results of erythromycin therapy in these 60 patients are summarized in Table I.

Infections caused by staphylococci. There were 26 patients in this group. Twelve patients had infections of soft tissues with or without abscess formation, and 10 of them showed a good or excellent response to erythromycin therapy. One patient who did not respond had a severe chronic recurrent furunculosis of both buttocks. She was given a total of 52 grams of erythromycin over a period of 1 month. Erythromycin-resistant staphylococci were recovered at the end of the treatment. The other patient who showed no response had pustular acne.

Eight patients had bone infections including acute and chronic osteomyelitis and infections secondary to operative procedures on bone. Five out of these 8 patients showed good results with erythromycin therapy. The sixth patient received 2 weekly courses of therapy, and there was an estimated 80 per cent clearing of the infection in a postoperative fenestration cavity with infectious dermatitis of the auricle and bearded portion of the face on the operative side. It could not be determined how much the clinical course of this infection was influenced by erythromycin therapy and the result is classified as equivocal. The seventh patient had chronic osteomyelitis of the left tibia with a draining sinus. Although the causative organisms were very sensitive to erythromycin in vitro, the infectious process was not influenced, presumably because of the impoverished blood supply to the lesion. The eighth patient had a chronic, recurrent infection of a fenestration cavity. A first course of erythromycin therapy cleared the infection for 1 month with subsequent recurrence. The second course had no effect. The staphylococci were erythromycin-resistant.

The remaining 6 patients had relatively more severe infections: Two were cases of staphylococcal epidural abscess following operation for cerebrospinal fluid rhinorrhea, and craniotomy for brain tumor respectively. In spite of good clinical responses, the results of erythromycin therapy were considered equivocal inasmuch as other antibiotics were administered in addition to erythromycin. In these 2 cases it is impossible to credit the beneficial antibiotic effect to either erythromycin or the other antibiotics administered. The third was a case of a staphylococcal empyema of the left side subjected to an open thoracotomy drainage. Although this patient improved clinically during the period of treatment, the improvement cannot be attributed to erythromycin therapy in view of the persistent exudate from which erythromycin-resistant staphylococci were recovered in increasing numbers. The fourth was a case of a postpartum septicemia, due to a hemolytic Staphylococcus aureus following a generalized dermatitis. The patient was treated with a 600 milligram dose of erythromycin every 4 hours for a period of 28 days for a total dosage of 96 grams after previous penicillin and streptomycin therapy was ineffective. The causative organism was resistant to penicillin,

TABLE I.—ERYTHROMYCIN THERAPY

	Days	Dose (grams)	Clinical results				
			Total No. of patients	Excellent	Good	Equivocal	No response
Infections caused by staphylococci							
Soft tissue (hand, cellulitis, abscess)	4 to 34	5 to 50	12	2	8		2
Bone (osteomyelitis, fenestration cavity, mandible reconstruction)	4 to 16	5 to 20	8		5	1	2
Epidural abscess	26	20	2			2	
Empyema	42	67	1				1
Septicemia, postpartum	28	96	1	1			
Pericholangitis	13	21	1		1		
Enteritis	4	5.2	1	1			
			26				
Infections caused by streptococci or by streptococci and staphylococci							
Subacute bacterial endocarditis	19	34	1				1
Cellulitis, lymphangitis	5 to 7	8 to 13	3	2	1		
Reconstruction of mandible	9	17	1			1	
			5				
Genitourinary tract infections							
Acute prostatitis	5	10.4 to 11.4	6	2	2		2
Chronic prostatitis	5	9.6 to 10.4	13		5	3	5
Acute epididymitis	5	10.8	1	1			
Prostatovesiculitis	5	11.4	1				1
Glomerulonephritis with pyelonephritis	6	7.2	1				1
			22				
Infections caused by gram-positive cocci and gram-negative bacilli							
Infected burns—30 per cent body surface	6 to 10	12 to 18	2		1		1
Postmastoidectomy perchondritis of auricle	4	4.8	1			1	
Infected colostomy wound, adenocarcinoma of colon	19	38.8	1			1	
Gluteal abscess, lymphatic leukemia	18	17	1			1	
Infected amputation stump	6 to 29	2.4 to 23	2				2
			7				
		Totals	60	9	23	10	18

streptomycin, and the broad spectrum antibiotics, but sensitive to erythromycin. With the beginning of erythromycin therapy the temperature returned to within normal limits in 3 days. In this same period the blood culture became sterile and all subsequent blood cultures were negative. The result in this case was considered to be excellent. The fifth was a case of a hemolytic staphylococcic postcholecystectomy pericholangitis with T-tube drainage of the common duct. The diagnosis was confirmed by liver biopsy. Prior treatment with oxytetracycline and streptomycin was of no avail. Erythromycin therapy was begun. A total dose of 21 grams was administered over a period of 13 days. The blood serum level of erythromycin exceeded 0.625 microgram per milliliter while the concentration in the bile was approximately 20 micrograms per milliliter. The temperature fell to normal on the fourth day, and liver function tests reverted slowly to normal. Since cessation of therapy there has been no recrudescence of fever or of jaundice. This is considered to be a good result. The sixth and final case of the first group consisted of a severe gastroenteritis following treatment of a persisting pneumonitis with penicillin, chlortetracycline, oxytetracycline, and streptomycin. Stool culture from this patient re-

vealed a pure culture of Staphylococcus aureus which was resistant to penicillin and the broad spectrum drugs. This patient was given 5.2 grams of erythromycin therapy over a period of 4 days. There was a prompt reversion of the temperature to normal and a prompt subsidence of diarrhea in this patient who was first seen in a choleriformic condition. The patient was able to tolerate a regular diet on the fourth day of erythromycin therapy. A stool culture on the fifth day revealed a return of Escherichia coli to the stools. The response in this case is considered excellent.

In summary, 18 of 26 patients with staphylococcal infections were considered benefited by erythromycin therapy. Failures were associated with emergence of drug-resistant organisms or the nature of the lesion.

Infections caused by streptococci or by streptococci and staphylococci. There were 5 patients in this group. The first patient with subacute bacterial endocarditis had been treated previously for a year with massive doses of streptomycin, penicillin, chloramphenicol, oxytetracycline, and bacitracin. At the time that erythromycin therapy was instituted the alpha hemolytic streptococcus was found to be resistant to penicillin, chlortetracycline, oxytetracycline, and chloramphenicol. The sensitivity to erythromycin was 0.4 microgram per milliliter. The patient was given 300 milligrams of erythromycin every 4 hours, with demonstrable blood serum levels ranging between 1.25 to 2.5 micrograms per milliter. This patient failed to respond and died on the nineteenth day of therapy. At necropsy, profuse vegetations of the aortic valve with perforation of the aortic valve cusps and acute cardiac dilatation were found. The second, third, and fourth patients were cases of cellulitis. The first of these, with an infected blister of the great toe with regional lymphangitis and inguinal lymphadenitis, responded dramatically to a total dose of 9.6 grams of erythromycin given over a period of 6 days. The second case exhibited cellulitis of the extensor surface of the left hand with lymphangitis and lymphadenitis of the left axilla and showed an excellent response to 8 grams of oral erythromycin given over a period of 5 days. The third case of cellulitis was a patient with a web space infection between the fourth and fifth toes with inguinal lymphadenopathy and responded more slowly than the other 2 patients. He received 12.8 grams of the drug over a period of 9 days. The fifth and last patient with an infected mandibular bone graft showed an equivocal response to erythromycin therapy administered in a total dose of 16.8 grams over a period of 9 days. The inflammatory reaction cleared but the exudate continued to grow Staphylococcus aureus and Streptococcus fecalis although both were erythromycin sensitive. Suppuration ceased after chloramphenicol therapy was instituted.

In summary, out of the 5 patients in this group, 3 showed a good response to the treatment, 1 showed an equivocal response, and 1 did not respond at all.

Genitourinary tract infections. There were 22 patients in this group. None had benign prostatic hypertrophy or other urinary tract obstructions. None had acute gonococcal infections. There were 6 patients with acute prostatitis. Two of them showed an excellent response and 2 others showed a good clinical response with apparent cure. The 2 remaining patients were unaffected by erythromycin therapy. One had Streptococcus fecalis moderately sensitive to erythromycin and the other gram-negative bacilli which were erythromycin-resistant. There was 1 case of acute epididymitis which responded dramatically and apparently completely to erythromycin therapy within 3 days. There were 13 patients with chronic prostatitis, of which 5 showed good immediate clinical responses, 3 showed equivocal responses, and 5 others showed no response. The failures were associated with recovery of erythromycin-resistant organisms in the urine or prostatic secretions. Some of the patients showing apparently good or equivocal responses developed recurrences at a later date. There was 1 case of prostatovesiculitis which showed no clinical response and no change in the urinary flora while on erythromycin therapy. The last patient of this group had glomerulonephritis and superimposed pyelonephritis. The following organisms were cultured from

the urine: Streptococcus fecalis, Aerobacter aerogenes, Pseudomonas aeruginosa and Staphylococcus aureus. Erythromycin therapy was instituted in addition to penicillin and streptomycin. The patient died on the fifth day of therapy from the glomerulonephritic process. With the exception of the last mentioned, all patients were treated for a period of 5 days and were given a total dose of erythromycin ranging from 9.6 to 11.4 grams, in addition to massage and heat therapy.

Mixed infections caused by gram-positive cocci and gram-negative bacilli. There were 7 patients in this group. One patient had 2 months old granulating infected burns involving 30 per cent of the body surface from which hemolytic Staphylococcus aureus and pseudomonas organisms were cultured. Previous attempts at skin grafting were only partially successful in spite of vigorous supportive measures and penicillin and streptomycin therapy. The staphylococci were erythromycin sensitive. Erythromycin therapy was instituted orally and also topically at the time of skin grafting. There was a more than 90 per cent primary take of the grafts. The patient improved remarkably thereafter. There were no adverse local phenomena attributable to topical therapy. This is considered to be a good result of erythromycin therapy. Another patient with 30 per cent burns of the body and with suppurating unsequestrated burn eschar did not benefit from intensive oral erythromycin therapy. The following organisms were cultured from the unsequestrated burn eschar: Staphylococcus aureus, Aerobacter aerogenes, and Pseudomonas aeruginosa.

The third patient had a postmastoidectomy perichondritis of the auricle on the side operated upon. Pseudomonas aeruginosa and Staphylococcus aureus were grown from the wound exudate. Erythromycin therapy was instituted with resolution of the infection and nearly complete healing of the aural lesion. The same organisms, however, were grown repeatedly from the mastoid cavity which did not heal completely. The result is classified as equivocal.

The fourth patient developed infection in a laparotomy wound following hemicolectomy for adenocarcinoma of the ascending colon. During the period of erythromycin therapy (38.3 gm. over a period of 19 days) the cellulitis resolved slowly. The temperature fell to near normal limits, but the character and bacteria of the discharge were essentially unchanged. The wound tract was explored and found originating in a small ileal fistula which was resected. The abdominal wound healed after delayed primary closure.

The fifth case was a young adult patient with acute lymphatic leucemia who developed a deep abscess in the right gluteal region. Culture of the pus revealed Staphylococcus aureus, pseudomonas, and proteus organisms. Erythromycin therapy was begun, and the clinical impression was that this therapy helped to localize an infection which otherwise might have spread rapidly and metastasized. On the nineteenth day of therapy the patient died suddenly of a gastrointestinal hemorrhage. At necropsy, partial healing of the abscess was observed. The response in this patient is considered to be equivocal.

There were 2 cases of infected amputation stumps. Wound cultures revealed the presence of Staphylococcus aureus and proteus in one case and Staphylococcus aureus, Pseudomonas aeruginosa, and proteus in the other. Erythromycin therapy failed to produce any lasting benefit in either of these.

In summary then out of the 7 patients in this group, 1 showed a good response to the treatment, 3 showed an equivocal response, and 3 showed no response.

DISCUSSION AND SUMMARY[1]

In all of these patients, the blood serum levels which were measured following the administration of erythromycin were adequate for erythromycin-sensitive organisms against which they were employed. A possible exception was Streptococcus fecalis in the prostatic secretions when concentrations in the prostate

[1]Since this paper was submitted, Herrell and associates (*J. Am. M. Ass.*, 1953, 152: 1601–1606) reported their experiences with erythromycin in 54 patients with various types of staphylococcal infections, which are in agreement with ours: This antibiotic was successful in staphylococcal ileitis, meningitis, and throat and urinary tract infections, as well as in 6 of 8 cases of staphylococci bacteremia and in about one-half of 17 cases of infections of the skeletal system and soft tissues. In some cases failure was attributable to drug resistance, and in some to other causes.

gland were lower than in the blood. We have confirmed the observations of others that erythromycin is excreted in the unobstructed biliary system in higher concentrations than in the blood serum. The only untoward effects of erythromycin therapy noted were gastrointestinal disturbances which consisted of epigastric pain, nausea, or mild diarrhea. These complications occurred in 13 of the 60 patients (21 per cent). None were severe enough to warrant cessation of erythromycin therapy. The impression was gained that these reactions were fewer and less severe when the drug was administered in enteric-coated tablets rather than in gelatin-coated capsules.

Many of the patients treated with erythromycin showed no clinical response to penicillin or the broad spectrum drugs. Thirty-two of these (53 per cent) were benefited by erythromycin; i.e. they had an excellent or good response, while 28 (47 per cent) had an equivocal or no response. Of the staphylococcal infections treated, 70 per cent were benefited. Erythromycin therapy was found to be beneficial when the causative organisms were erythromycin-sensitive in early soft tissue infections, acute infections in bone with a good blood supply, septicemia, pericholangitis with adequate drainage of the biliary tree, acute prostatitis, acute epididymitis, and staphylococcal enteritis. Erythromycin therapy was of little or no benefit in soft tissue infections caused by erythromycin-resistant organisms, mixed infections containing erythromycin-resistant bacteria, infected wounds with unsequestrated necrotic tissue, late subacute bacterial endocarditis, chronic prostatitis, and empyema.

Erythromycin appears to be a useful short term drug for treatment of pyogenic surgical infections caused by sensitive organisms in loci where the blood supply is adequate and necrosis is absent or not extensive. Favorable response is apparent within 72 hours of treatment although treatment may be necessary for longer periods. Prolonged therapy may be associated with the appearance of drug-resistant forms. If no benefit is observed clinically by 5 days, continued therapy is likely to be of no avail. Use of this drug, like any other antibiotic, is adjunctive to surgical intervention when necrotic foci are present. Erythromycin therapy deserves further trial in staphylococcal infections when the organisms are resistant to other antibiotics, or when, for one reason or another, the patient cannot tolerate therapy with them. Combination therapy for mixed infections requires further investigation.

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CARCINOMA OF THE LARGE INTESTINE

A New Approach to the Study of Venous Spread

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CARCINOMA of the colon and rectum spreads by means of direct extension, peritoneal sedimentation, lymphatic metastasis, and by way of the blood vascular channels. The methods currently employed by the surgeon and the pathologist to estimate the degree of extension by the first three means are fairly accurate. In the equally, or even more, important matter of blood vascular spread, studies by histologic methods have never given results corresponding with the known frequency with which blood vascular channels disseminate cancer cells. Thirty per cent of patients undergoing laparotomy for supposedly curable carcinoma of the rectum and colon reveal metastasis to the liver, but by no means do all of these lesions exhibit major or even minor lymphatic involvement. Nearly 50 per cent of those patients whose growths have been surgically removed with hope of cure reveal evidence of, and finally succumb to, the effects of hepatic and other visceral metastasis usually because of blood-borne dissemination of their disease.

Prompted by these facts, a new method of approach was employed to study intravascular involvement in spread of carcinoma of the colon and rectum. As compared with that shown by the routine histologic techniques an increased incidence of intravascular spread demonstrated by this method gave useful information on which to base prognosis in the immediate postsurgical period. Subsequently a 5 year follow-up study is contemplated to determine the validity of the assumption that positive evidence of vascular spread in the studied specimens is reflected in terms of eventual outcome.

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Abridgment of thesis submitted by Dr. Barringer to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

HISTORICAL REVIEW

Broders' (1, 2) microscopic method of grading carcinoma, described in 1920 and modified in 1925, and Dukes' (6) method of gross classification of cancer of the rectum were two of the first and most important advancements relative to the activity, extension, and prognosis regarding malignant growth. Thirty per cent of colonic carcinomas seen at the time of operation are incurable because of the presence of metastasis in the liver. The methods of classification already mentioned do not take into account the problem of blood vascular spread of the malignant process which is probably alone responsible for hepatic involvement.

The most common site for visceral metastasis is the liver. The lungs are second, and the adrenals, bone, thyroid, kidney, intestine, spleen, and pancreas follow in the order named. The ovary, heart, skin, gallbladder, colonic stoma, brain, appendix, and pleura are occasionally involved. Out of 170 patients coming to necropsy from the effects of colonic carcinoma Brown and Warren found a total of 70 with visceral metastasis; 57 of these 70 exhibited hepatic metastasis and only 38 had pulmonary spread. In only 3 patients of this group did blood-borne metastasis take place without concomitant spread to the liver or lung. The probable mode of dissemination in these 3 patients was by way of Batson's paravertebral veins.

Approaching the problem from a histologic angle, Grinnell used Masson's aniline blue trichrome stain for study of the sections. He found blood vascular invasion most frequently in the fat and connective tissue outside the muscularis propria and next most frequently

in the submucosa. Definite intravascular invasion was found in 36 per cent of the cases studied. Grinnell referred to the high incidence obtained by Brown and Warren (41 per cent) as being due to the fact that the majority of their specimens were taken from necropsy material in advanced cases in which no operation had been attempted. Involvement of the large veins appeared more likely to be associated with distant metastasis than did invasion of smaller ones. He maintained that metastasis did not occur until the tumor had first penetrated the muscular coats of the bowel. In 90 per cent of 30 operative specimens with known visceral metastasis, invasion of blood vessels was found. (Brown and Warren had found vascular involvement in all but 1 case in which there was visceral metastasis.)

Coller, Kay, and MacIntyre found an incidence of 15 per cent of blood vessel involvement in carcinoma of the rectum and stated that "hematogenous spread is at present an unpredictable factor." In 1 of their "positive" cases, a neoplasm measuring only 2 centimeters in diameter had infiltrated just to the muscularis propria; it was a moderately well differentiated adenocarcinoma mucosum of grade 2 malignancy. Yet, judged by clinical criteria, this patient should have had a good prognosis. In their series the degree of malignancy was not a determining factor in the occurrence of hematogenous metastasis for, of their specimens in which metastasis was found microscopically, 6 lesions were graded 2, 1 was graded 4, and 1 was a spindle-cell sarcoma. Two lesions had invaded blood vessels but had established no lymphogenous metastasis.

Sunderland studied two series for a combined total of 210 cases and searched for venous invasion. His tissues were stained with Weigert's elastic tissue stain followed by alum or iron hematoxylin and van Gieson's stain. Positive results were observed in about 28 per cent of the total. He found that the small and medium-sized vessels were most frequently involved and that there was a definite increase in venous invasion with increased carcinomatous penetration of the bowel wall and with the occurrence of lymphatic spread. Almost half (42.6 per cent) of the tumors situated 6 centimeters or less above the anus invaded veins, as compared to 22.2 per cent of those 6 to 12 centimeters above and 5.9 per cent of those more than 13 centimeters above. The prognosis for patients whose carcinomas showed vascular invasion microscopically was definitely worse than for those whose carcinomas did not exhibit this mode of spread. The survival rate of patients whose carcinomas had metastasized to lymph nodes was almost three times as high when venous invasion was not also found (57.7 per cent) as when it was found (20 per cent). It was very properly suggested that routine search for venous invasion may give information that will be of prognostic value.

ANATOMIC CONSIDERATIONS

The distribution of the veins of the large bowel is almost identical with that of the arteries of this region except for the addition of the inferior mesenteric vein and the fact that in many instances 2 small veins accompany one larger artery. There is no set venous pattern of distribution but in general the veins follow a similar arrangement throughout the entire large bowel.

The hemorrhoidal plexus surrounds the rectum, communicating anteriorly with the vesical plexus in the male and the uterovaginal plexus in the female. It consists of an internal network in the submucosa and an external network outside the muscular coat. These two networks are intimately connected with each other by many small anastomosing radicles perforating the muscular layer of the bowel wall. Immediately above the anal orifice and connected by transverse branches the internal network forms a series of dilated pouches which are circularly arranged around the lumen of the bowel.

The lower part of the external plexus is drained by the inferior hemorrhoidal veins into the internal pudendal vein; the middle part by the middle hemorrhoidal vein which joins the hypogastric vein; and the upper part empties into the superior hemorrhoidal vein which forms the inferior mesenteric vein at a higher level. This in turn is a tributary of the splenic branch of the portal vein. A free com-

munication between the portal and the systemic venous systems is established through the hemorrhoidal plexus.

The inferior and middle hemorrhoidal veins vary in number from 1 to 5. The middle hemorrhoidals are often so small as to be almost unidentifiable under which circumstances the superior hemorrhoidal vein often arises directly from the hemorrhoidal plexus.

The terminal veins of the sigmoid, descending, and splenic portions of the colon are distributed in essentially the same manner as the terminal veins of the cecum, ascending, hepatic, and transverse portions of the colon and will be discussed together. They drain into the marginal vein which empties into the sigmoidea ima and sigmoidal veins, left ascending and descending colic veins which merge to form the inferior mesenteric vein, this emptying into the splenic (lienal) vein. The ileocolic vein (its branches: the ileal, appendiceal, anterior, and posterior cecal), right colic (ascending and descending branches), and the middle colic, with its right and left colic branches, empty into the superior mesenteric vein which joins with the splenic (lienal) vein to form the portal vein. There are extensive anastomoses between the superior and inferior mesenteric veins in the region of the splenic flexure, which are referred to as arcades and have their convexity directed toward the bowel wall. The marginal vein is found nearest the bowel wall.

The terminal veins arise from an extensive plexus of venules in the submucosa with their branches penetrating the muscularis at which point they are divided into two general groups: (1) the long branches which arise from the antimesenteric border near the distal longitudinal bands and course just deep to the serosa to join the marginal vein and (2) the short branches which arise in the mesenteric or proximal border and lie primarily in the serosal layer of the mesocolon. Occasionally, these join the marginal vein but usually they enter the long branches prior to their anastomosis with the marginal vessel. The short branches are more numerous than the long ones. Anastomoses between these vessels are extremely rare; however, occasionally two branches may join before they enter the marginal vein. The general course of the terminal veins is perpendicular to the axis of the colon.

The portal vein is a short large venous trunk that is formed by the union of the superior mesenteric and the splenic (lienal) veins. At the upper border of the pancreas it enters the hepatoduodenal ligament lying posterior to the hepatic artery and bile duct. It divides into two branches which enter the porta of the liver. It is the afferent vessel of the liver and carries to the liver the venous blood from all of the unpaired organs of the abdomen, that is, the digestive tract, including the liver and pancreas, and the spleen. The inferior mesenteric vein opens into the splenic (lienal) vein or more rarely (10 per cent) into the superior mesenteric vein.

MATERIAL AND METHODS

Permission for examination of the specimens for this study was granted by the attending surgeon and the fresh material was obtained at the time of operation from 45 patients with carcinoma of the large intestine. In 43 instances the lesions were excised with hope of cure for there was no gross evidence of visceral spread. Two lesions were associated with verified metastasis to the liver and these were also subjected to the procedure detailed in a succeeding paragraph to test its value in known cases of blood vascular spread. No other carcinomas removed for "palliation" were studied inasmuch as we were interested chiefly in the group of individuals with possible venous spread as a factor working against an otherwise good prognosis. There were 19 female and 26 male patients, their ages varying from 21 to 73 years. Eight were under the age of 55 years, their ages being 21, 34, 36, 39, 42, 48, 48, and 53 years respectively.

The venous bed of the large bowel studied in this investigation included that of the cecum, ascending, hepatic, transverse, splenic, descending, and sigmoid portions of the colon, and the rectum removed by one stage anterior resection, and by one stage or two stage combined abdominoperineal resections for involvement by carcinoma. The attending surgeon, where feasible, expedited the injection by leaving long fishline ligatures on one or more of the larger veins. The specimens were

hen taken directly from the operating room o the laboratory where the following pro-edures were carried out.

Solutions for injection. A saturated aqueous olution of lead acetate was used for the first examinations; however, brominol (light) was ound to be the most satisfactory solution for oentgenographic reproduction of the venous ed. One cubic centimeter of methylene blue 2 per cent aqueous solution) was added to the rominol to outline the vessels more clearly in he gross specimen. The injection was facili-ated by warming the syringe containing the rominol under the hot-water spigot in the aboratory, because of its decreased viscosity t a higher temperature.

Preparation and injection of the specimen. he lumen of the bowel was washed with cold ap water and the largest vein was cannulated ith an 18 gage needle. Some difficulty was ccasionally encountered in finding a vein rge enough for satisfactory cannulation. he venous bed was perfused with cold tap ater to flush out the remaining blood. The apillaries and small vessels in the resected order of the mesentery on the operative spe-imen were then secured with a running cotton uture to prevent leakage at the time of the rominol injection. The lumen of the resected pecimen of bowel was filled with water and he ends closed with heavy cotton ligatures. All major vessels in the resected specimen were ligated with No. 40 cotton thread and marked. To the needle which had been used o flush out the remaining blood in the speci-men an ordinary 20 cubic centimeter glass syringe filled with the warm brominol solu-tion described was attached. This solution was injected into the lumen of the vein until the venous bed of the specimen was distended to the approximate degree seen at the operat-ing table. Manometric readings were not taken. The vein was then ligated just beyond the point of the needle and the latter was re-moved. Water from the cold tap was then al-lowed to run freely over the injected specimen to wash off the brominol that might have leaked from the severed capillaries and to in-crease the viscosity of the brominol. This re-sulted in blockage of the capillaries and pre-vented further leakage from them. The in-jected specimen was then placed on paper towels for "adsorption" of the wash water and any additional leakage from the inter-rupted capillaries.

TABLE I.—MICROSCOPIC VENOUS INVOLVEMENT VERSUS RADIOGRAPHIC VENOUS INVOLVE-MENT ACCORDING TO LOCATION OF LESION

Location	Specimens studied	Microscopic venous involvement	Radiographic venous involvement
Cecum	2	1	1
Ascending colon	3	1	1
Hepatic flexure	1	1	1
Transverse colon	2	2	1
Splenic flexure	2	1	2
Descending colon	3	0	0
Sigmoid colon	14	3	8
Rectum	18	8	9
Total	45	17	23
Percentage of total	100	38	51

No attempt was made to determine the number of associated lymph glands removed with the gross specimen by means of dyes or India ink injections. Neither the gross speci-men nor the blocks of tissue removed for sec-tioning were cleared for this purpose.

Roentgenographic examination and study. Immediately prior to taking the roentgeno-grams the specimen was transferred to a cleared x-ray film for handling and roentgeno-grams were made from two angles, namely, anteroposterior and lateral; a number were also made stereoscopically. The roentgeno-grams were examined while wet. The venous bed was thoroughly studied from the growth to the most proximal portion of the resected specimen and a careful search was made for evidence of blocked or thrombosed vessels. The vein or veins which appeared to be ob-structed were marked by placing straight pins in the respective locations and blocks of tissue about 0.5 by 1 centimeter were removed from all areas revealing evidence of occlusion. There were never more than 3 such areas and generally only 1 or 2 which were suitable for examination and study.

Microscopic examination and study. The several blocks of tissue taken from the course of the veins in the suspected areas were then

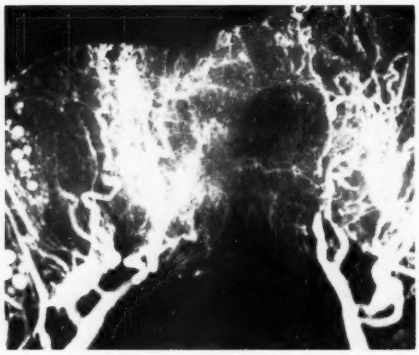


Fig. 1. Negative roentgenographic evidence of venous spread of carcinoma of the large bowel. There is no evidence of obstruction in the venous bed. Multiple blocks were taken throughout the area of the lesion and sections from them were stained with polychrome methylene blue (frozen section technique), hematoxylin and eosin, van Gieson's elastic tissue, and Masson's trichrome stains. All sections were negative for venous involvement by carcinoma tissue. The gross lesion measured 8 by 6 by 2 centimeters and was grade 2 (Broders) and group B (Dukes).

examined by the frozen section technique, the sections being stained with polychrome methylene blue.[1] The blocks which showed indication or possibility of venous involvement were saved for permanent staining with hematoxylin and eosin, van Gieson's elastic tissue stain, and Masson's trichrome stain. Table I gives the positive and negative findings for both the microscopic and radiographic methods of examination. Typically negative roentgenographic findings are shown in Figure 1. In Figure 2 is seen typically positive roentgenographic evidence of venous involvement by carcinoma. Blocks sectioned from these areas revealed carcinoma microscopically within the lumen of the veins. All questionable microscopic sections were counted as giving negative results and the criteria were based on the presence of the elastic membrane and the muscular wall. Lymphatics of a size sufficient to be confused with small veins were not believed to be, nor found to be, present in the areas from which the blocks removed for sectioning were taken.

[1]The polychrome methylene blue stain rendered an invaluable service with its speed and efficiency in staining the frozen sections; nevertheless there were, at times, questionable areas necessitating final proof with the permanent stains listed.

RESULTS

Figure 2 shows the areas in the specimens from which the blocks of tissue were taken to make the sections. In Figure 2a is shown the blocked vessel from which the photomicrographs in Figure 3 were made. The roentgenograms in Figure 2b, c, and d correspond to the photomicrographs in Figures 4, 6, and 7 respectively. Figures 3 to 7 present evidence of venous spread.

The sections in 17 of the cases (38 per cent) showed venous involvement when studied by the microscopic method. All but 1 of the microscopically positive specimens showed evidence of venous involvement by the roentgenogram. Twenty-three (51 per cent) of the specimens studied revealed venous occlusion by roentgenography, 2 specimens (5 per cent) were considered doubtful and were counted negative, making a total of 49 per cent negative. Thus 7 more specimens gave positive results by the roentgenographic method than by the microscopic method. This discrepancy will be discussed later.

Microscopic and roentgenographic evidence of venous involvement as related to the grade (Broders' method) and group (Dukes' classification) of the lesions was determined. The entire group of lesions was classified by Dukes' method, regardless of the location, for matters of simplification and a more satisfactory comparison. Fourteen (31 per cent) were of grade 1; 27 (60 per cent) of grade 2; 3 (7 per cent) of grade 3; and only 1 (2 per cent) of grade 4; whereas, 2 (4 per cent) were of Dukes' group A; 30 (67 per cent) of group B; and 13 (29 per cent) of group C (Table II).

Six out of the 14 grade 1 lesions exhibited both microscopic and roentgenologic evidence of venous spread, an equal number gave negative evidence to both methods, and 2 gave negative microscopic but positive roentgenologic evidence. Of the 27 grade 2 adenocarcinomas, 8 gave positive results by both methods of study, 13 gave negative results by both, 5 gave negative microscopic but positive roentgenographic results; in 1 case there was positive evidence of venous involvement on microscopic study but negative results were obtained by the injection method. Two of the grade 3 adenocarcinomas studied gave

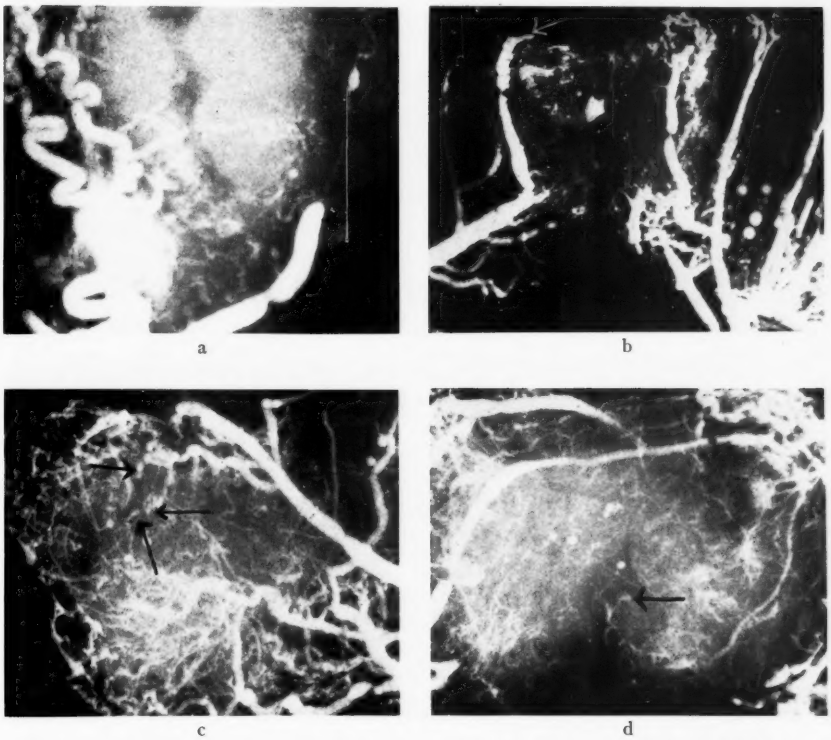


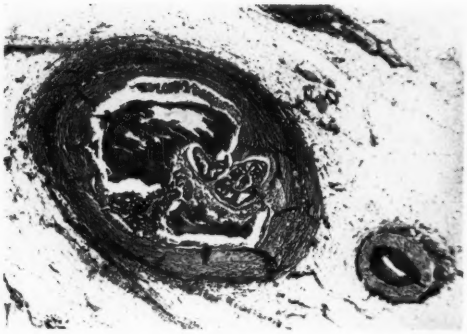
Fig. 2. Positive roentgenographic evidence of venous spread of carcinoma of the large bowel. a, One of the larger vessels (arrow) is occluded by carcinoma tissue. This was demonstrated by gross dissection. Microscopic sections from this site are shown in Figure 3a, b, and c. The gross lesion measured 8 by 6 by 2 centimeters, and was grade 1 (Broders) and group B (Dukes). b, Only partial occlusion of the involved vessel (arrow). A microscopic section is shown in Figure 4. The gross lesion measured 4 by 8 by 1 centimeters, and was grade 2 and group C. c, Multiple veins are occluded. A microscopic section from one of these is shown in Figure 6. The gross lesion measured 5 by 5 by 1 centimeters, and was grade 1 and group B. d, An occluded vessel, a microscopic section of which is reproduced in Figure 7. The gross lesion measured 7 by 6 by 2.5 centimeters, and was grade 1 and group B.

positive results by both methods and 1 gave negative results by each procedure. There was only 1 grade 4 lesion and it did not give evidence of venous involvement by either method.

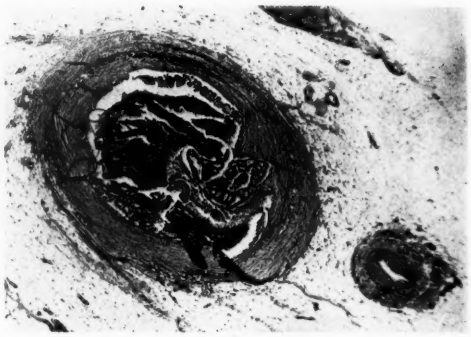
On the basis of Dukes' classification the A lesions were represented by only 2 cases. In 1 of these cases negative results were obtained by both methods of study, and in the other, positive results were obtained by the roentgenographic method only. In 30 cases the lesions were classified as B lesions; in 9 of these cases there was positive evidence of venous involvement microscopically and roentgenographically, in 17 the results were negative by both methods, and in 4 the results were positive by roentgenogram only. There were 13 cases in the C category. In 7 of these the results were positive by both methods, in 3 they were negative by both methods, in 2 they were negative microscopically but positive by roentgenogram, and in 1 they were positive on microscopic examination only.

COMMENT

Dissemination of carcinoma to distant parts of the body by the vascular system does not generally take place in the early stages of the



a



b

c

Fig. 3. Positive microscopic evidence of venous spread, ×13. The sections were taken from the site indicated in Figure 2a. The gross lesion measured 8 by 6 by 2 centimeters, and was grade 1 (Broders) and group B (Dukes). a, Van Gieson's elastic tissue stain was used to demonstrate the layers of the vein wall and the malignant tissue within the lumen. A small artery is also present but contains no carcinoma tissue. Compare this section with those in b and c for its superiority in demonstrating the vein wall and the carcinoma. b, Section stained with hematoxylin and eosin. The vessel with carcinoma in its lumen can be seen very easily; however, the walls of the vessel and its elastic membrane do not stand out in contrast as with van Gieson's stain. Compare with a and c. c, Section stained with Masson's trichrome methylene blue. Compare with a and b. It demonstrates the superiority of van Gieson's stain over this method. The superior stains bring the elastica into sharp contrast.

disease. It has been shown, however, that small lesions may metastasize early, the metastatic lesions outstripping the original lesion in size. Occasionally very large lesions remain local, metastasizing late, if at all.

In the development of blood-borne metastasis, whether in spontaneously occurring or transplanted tumors, there are two phases. The initial phase is that in which the tumor cells in the primary growth penetrate the endothelial layer from the outside. The transportation of emboli and their arrest are purely mechanical. The second phase which is critical for their establishment is that in which the tumor cells establish organic union with the vessel wall after their arrest, penetrating the endothelium from the inside. Before the second phase the tumor cells are bathed in blood plasma and serum; if clotting occurs they are exposed to the destructive action of the leucocytes. The endothelial surfaces present great resistance to the spread of growing tumors, as shown by Haaland, in 1905, in the Jensen mouse. Schmidt, in 1903, showed by study of the lungs in cases of generalized carcinoma in man that many emboli die in the vessels and, therefore, do not give rise to secondary growths. He pointed out the importance of thrombus formation in providing a new vascular connection between the tumor cells and the vessel wall and demonstrated that failure or delay of this was sufficient to ensure death of the transported tumor cells. Levin and Sittenfield, in 1911, injected saline suspensions of 2 rat sarcomas and a mouse tumor into the jugular vein of mice. These tumors grew well on subcutaneous inoculation but microscopic pulmonary nodules were rarely seen following intravenous injection. Many hyaline thrombi were found in the lungs of the injected mice, and others showed fibrous changes with occasionally a few "entrapped" and much altered tumor cells. Some tumor strains were very successful in implanting

TABLE II.—MICROSCOPIC VERSUS ROENTGENOGRAPHIC VENOUS INVOLVEMENT ACCORDING TO THE GRADE (BRODERS' METHOD) AND GROUP (DUKES' CLASSIFICATION) OF THE LESIONS

Grade and group	Microscopic and roentgenographic evidence of venous involvement				Cases	
	Both positive	Both negative	Micro. negative, roentgen positive	Micro. positive, roentgen negative	No.	Per cent
Grade						
1	6	6	2	0	14	31
2	8	13	5	1	27	60
3	2	1	0	0	3	7
4	0	1	0	0	1	2
Total cases	16	21	7	1	45	
Per cent of total	36	47	15	2		100
Group						
A	0	1	1	0	2	4
B	9	17	4	0	30	67
C	7	3	2	1	13	29
Total cases	16	21	7	1	45	
Per cent of total	36	47	15	2		100

themselves, while others failed to "take." Probably the closest approximation to spontaneous vascular metastasis was obtained in the "experimental massage" of a tumor by Tyzzer and Knox.

In 1904, Clogg noted that when dissemination occurred by way of the blood stream it frequently did so before the disease had spread to the lymph nodes. Recent studies have confirmed this impression and enlarged upon it to show that most vascular invasion originates within the intestinal wall or within the immediately adjacent perirectal tissues and not from the more distant extensions. Thus, even though a lesion is sharply limited, it may prove as deadly as the most widespread and perforating types. Venous invasion may occur at any stage in the development of carcinoma of the colon.

Warren and Gates, in 1936, came to the conclusion that the blood has no toxic effect on tumor cells even though only a small portion of those entering the circulation survive and grow in distant foci. Involvement of extravascular tissue rarely occurs by direct penetration of the arteriolar wall, but usually by growth through less resistant capillary walls and venules.

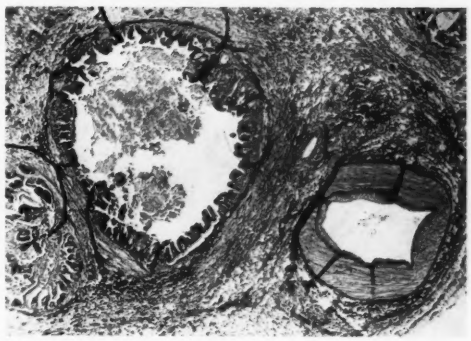
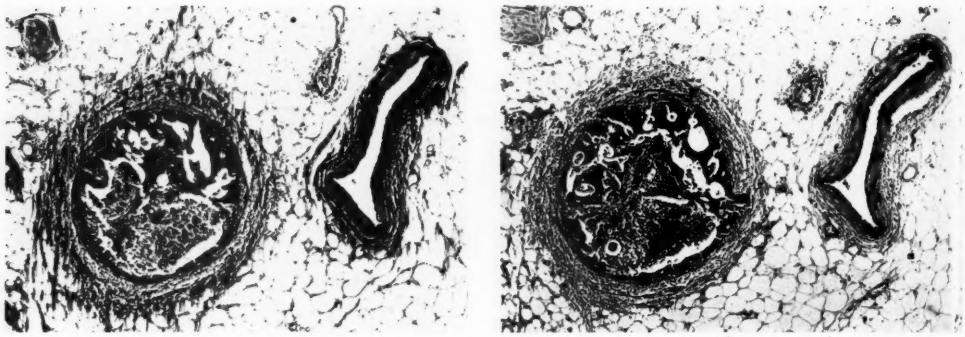


Fig. 4. Positive microscopic evidence of intravenous spread of carcinoma tissue (van Gieson's elastic tissue stain, ×19). The entire endothelial membrane of the vein has been replaced by a thick layer of carcinoma tissue that shows gland formation. The lumen is still widely patent and contains blood cells. An accompanying artery with no malignant involvement is shown. This section was taken from the site indicated in Figure 2b. The gross lesion measured 4 by 8 by 1 centimeter, and was grade 2 (Broders) and group C (Dukes).

Once carcinoma has spread into the venous channels with formation of malignant thrombi and dispersion of malignant emboli no surgical procedure, however radical, can be devised to cure the patient. Were such a sequence of events customary the prognosis for carcinoma of the rectum and colon would indeed be grave. Intravascular invasion, according to the literature, seems remarkably constant, occurring in approximately a fifth of all cases of malignant lesions of the lower part of the colon.

One of the most disappointing features in the end results of radical resection for carcinoma of the rectum and colon has been the frequent development of blood vascular metastasis. This is no reflection upon the efficiency of present surgical procedures designed to remove the primary growths, because a preoperative examination of the lungs and careful inspection of the liver at the time of laparotomy often reveal the presence of existing metastatic lesions. It has been shown by Mayo and Schlicke that the surgeon is able to determine the presence of hepatic involve-



a b

Fig. 5. Positive microscopic evidence of intravenous spread of carcinoma tissue, ×35. The gross lesion measured 5 by 7 by 2 centimeters, and was grade 3 (Broders) and group C (Dukes). a, Section stained with van Gieson's elastic tissue stain. Compare with the hematoxylin and eosin stained section in b for the selective merits of the two stains. Note that the lumen is not completely occluded. b, Section stained with hematoxylin and eosin. Compare with a for the selective merits of the two stains. Taken from the same block of tissue as that in a.

ment, at the time of laparotomy, with an accuracy of 91.7 per cent.

The radiographic injection method herein outlined for the demonstration of venous spread of carcinoma of the colon and rectum has several points in its favor. Manifest is the fact that it demonstrates in certain lesions interruption of the venous vascular continuity, alterations which could be interpreted as evidence of occlusion of these channels by the malignant process. Such vascular occlusion could occur as a result of external pressure on the veins, actual intravascular growth of the carcinoma cells, secondary intravascular clotting of the ordinary type, or a combination of all three. Proof has been afforded in this study that actual carcinomatous invasion of the vessels provided many examples of the abnormal vascular patterns. We believe that the chief merit in the method is concerned with directing the efforts of the examiner toward selecting tissue blocks most likely to be "positive" for venous involvement. With this in mind we are willing to accept as artefacts a goodly proportion of the roentgenograms exhibiting venous occlusion which could not be trans-

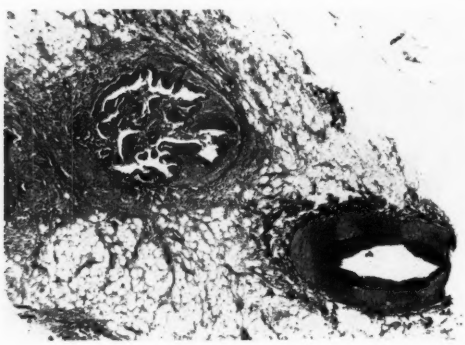


Fig. 6. Positive microscopic evidence of intravenous spread of carcinoma tissue (van Gieson's elastic tissue stain, ×19). A vein is shown with its lumen completely occluded and part of its wall destroyed by the malignant process that progressed from within outward. The accompanying artery is unaffected. This section was taken from the site indicated in Figure 2c.

Fig. 7. Positive microscopic evidence of intravenous spread of carcinoma tissue (van Gieson's elastic tissue stain, ×21). A vein with adenocarcinoma tissue in its lumen shows marked thickening and inflammatory reaction within its walls and the surrounding tissue. Note the perineural involvement and immunity of the small artery to malignant cells. Taken from site indicated in Figure 2d.

ated in terms of microscopic verification. Whether these artefacts will later prove to be erious prognostic features is a matter for future study when our patients have been followed for a long enough time post-operatively.

Polychrome methylene blue can be very advantageously employed in conjunction with apid frozen sections to segregate the tissue locks which give positive evidence of venous nvolvement. However, the stain of choice for ermanent record is unquestionably van Gieon's elastic tissue stain. It not only brings ut the endothelium and elastic membrane of he vessel in a clear manner but also reveals he muscular layers of the vessel as well as he malignant cells in a satisfactory manner. This finding is in accord with that of Sunderand. The sections stained with hematoxylin nd eosin would, on several occasions, have een read as negative had the venous involvement not been present so obviously with van Gieson's stain. Much the same can be said for Masson's trichrome stain as that for hemaoxylin and eosin; however, where there was narked destruction of the vessel wall, the ellular components of the blood were more atisfactorily revealed by this stain.

Identification of the vessels in the growth n the mucosal side of the bowel by staining nd microscopic examination is exceedingly ifficult because of their early and complete estruction. The more necrotic and eroded he lesion is found to be, the more prominently loes this fact stand out. The vessels become more distinct as one approaches the serosal surface of the bowel and frequently they are found to contain carcinoma cells within their lumen several centimeters away from the parent neoplasm and located in the perirectal fat and fatty connective tissue of the mesocolon. Some vessels were found to be only partially filled with carcinoma cells or to have been recanalized through the invading cell nests and again carrying a small amount of blood. These are the vessels that are looked upon with the greatest concern, for it is only reasonable to assume that from such vessels showers of malignant emboli may be released into the main venous channels of the portal system at frequent intervals, if not continuously (Figs. 4, 5, and 7).

SUMMARY AND CONCLUSIONS

The venous bed of the large intestine and rectum has been briefly described from the standpoint of the various possibilities of blood-borne metastasis to distant structures of the body. The portal system normally serves for venous drainage of the colon and upper two thirds of the rectum and thus the liver is the organ which is most vulnerable to venous metastasis, from cancer originating in viscera drained by the portal system. Previous microscopic examinations have revealed malignant cells within the veins at rates varying from 14 to 35 per cent and averaging about 20 per cent.

The literature has been reviewed and the general consensus is that nearly 50 per cent of the surgically treated patients that should be cured reveal evidence of, or succumb to, visceral metastasis within a 5 year period following operation.

A detailed description of a new method of examination, namely the roentgenographic visualization of the venous bed of the resected carcinomatous bowel by the injection of brominol, has been given.

Specimens in 45 cases of carcinoma of the large intestine were examined by the injection of a radiopaque substance into the venous bed and the making of roentgenograms of them. The venous outlines thus obtained were then carefully examined for obstruction of these vessels by the malignant growth. Twenty-three (51 per cent) were found, by means of this technique, to have 1 or more occluded vessels at some point either within or near the parent neoplasm in the surgically resected specimen.

Roentgenograms with accompanying photomicrographs of the occluded vessels are presented to show that malignant occlusion does occur and that it can be visualized by the injection of a radiopaque substance into the venous bed.

Specimens from the same 45 cases of carcinoma of the large intestine were carefully examined microscopically for evidence of venous invasion by carcinoma cells. Special staining methods were used for identification of the type of vessel invaded. Van Gieson's elastic tissue stain was found to be the stain of choice

in this regard. Seventeen specimens (38 per cent) were found to have venous involvement using the injection technique to direct selection of tissue blocks from the sites of presumed venous blockage.

Whether all patients with roentgenologically demonstrable venous blockage are potential candidates for blood-borne metastasis is a problem to be resolved by follow-up studies.

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THE TREATMENT OF CHRONIC OSTEOMYELITIS

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THE ALMOST miraculous alteration in the prognosis of acute osteomyelitis which followed the introduction of penicillin has not been matched by a similar change in the prognosis of established chronic osteomyelitis. This has been reflected in the spate of articles on the chemotherapeutic treatment of acute osteomyelitis compared with the very few recent papers on the treatment of chronic osteomyelitis.

We no longer find many patients suffering from intractable and persistently recurrent chronic osteomyelitis in the wards (or on verandas) of hospitals, and especially of children's hospitals. Nevertheless, there are still a few patients in whom treatment has included routine doses of antibiotics and in whom chronic infection follows an acute hematogenous osteomyelitis. Occasionally, chronic osteomyelitis also follows a compound fracture due to a gunshot wound or other injury, but in these cases such chronicity is more often than not related to incomplete primary treatment of the wound. Adequate débridement of compound fractures will remove all potential and actual foci of infection. Thus, infected thrombi which might extend the infection should not occur, and, as a result, osteomyelitis is less likely to become established. The necessity for adequate débridement was discussed by Scheman and associates who emphasized the point that bacterial infection alone does not produce osteomyelitis; it must lodge in a receptive soil.

As an example of the great change in the outlook of patients with compound fractures due to gunshot wounds which has been brought about by penicillin the following case may be quoted:

T.L., 21 years of age, was admitted to an Australian Casualty Clearing Station in 1945 seven days after receiving a compound fracture of the left femur due to a light machine gun bullet. During these 7 days no treatment was received, and when first examined the wounds were grossly infected. Under pentothal anesthesia the wounds were enlarged, obvious foreign bodies and sloughs removed, pockets of pus drained, extension was applied, and penicillin given in doses of 50,000 units third hourly. Within 6 weeks the wounds were firmly healed and were not inflamed. Eventually, he was left with some wasting of the left quadriceps, due mainly to the loss of muscle at the time of the original injury, and with an inch of shortening of the femur. After 16 weeks the union of the femur was sufficiently firm to bear his weight, and there was no limitation of movement of the left knee. In the years since then there has been no evidence of residual infection. Without chemotherapy union would have been even slower and an intractable infection would have been almost inevitable.

Although the risk of metastatic abscesses and toxemia may be greatly lessened in chronic cases by various antibiotics, once it has developed chronic osteomyelitis is still nearly as troublesome as formerly. However, the exhibition of antibiotics together with appropriate surgery may relieve the signs and symptoms of exacerbations of the infection; yet, no matter what antibiotic or group of antibiotics is chosen, operation still does not always abolish the infection. The organisms in the sclerosed and almost avascular bone enjoy a relative immunity for, unless widely exposed by operation, they are protected from an adequate concentration of these drugs. The normal protective inflammatory reactions are hardly to be expected in such unsuitable tissue. This is especially so under the condition of pressure and thrombosis which exist in the bone in chronic osteomyelitis and which so reduce the blood supply of the affected parts of the bone. It is to be noted that pockets of pus, even in the soft tissues of the body, respond poorly to chemotherapy; and, it is not surprising that this response is even poorer in bone. In addition to the inaccessibility of the organisms there is the problem in chronic bone infections of the special measures required to obliterate the space remaining in the bone after providing proper drainage and after removing the infected, sclerotic bone. Further,

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Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Although there had been a persisting sinus with recurrent exacerbations of inflammation, the removal of the sequestrum over the posterior aspect of the femur resulted in a disappearance of all evidence of active infection, and operative procedures on the shaft of the femur itself were not called for. In this case the chronic infection had followed a compound fracture.

Fig. 2. A chronic localized abscess in the lower end of the tibia following shrapnel wounds of the lower leg and tibia. After excision of affected portion of the bone, filling with cancellous bone chips, and the application of a cross leg flap, there has been no evidence of activity of the infection for more than 6 years.

Fig. 3. A chronic localized abscess in the lower end of the femur which became quiescent after the administration of penicillin in doses of 50,000 units every 3 hours for 4 weeks and which has not become reactivated after more than 6 years.

there is the fact that some of the infecting organisms or secondary invaders, for example, Bacillus pyocyaneus and Bacillus proteus, respond so poorly to chemotherapy.

Of recent years there has been a return of the use of more extensive operations in the treatment of chronic osteomyelitis for, combined with chemotherapy, the risk of spreading the infection has been greatly reduced and the chance of having the disease become quiescent permanently is much better than in the past. In any method of treatment, however, it will be acknowledged that sequestrectomy is still the most important single step (Fig. 1).

Apart from increasing the difficulty of eradicating the infection the scarring around an area of chronic osteomyelitis may be so dense as to interfere with operations for repair of injured nerves and even with operations for the correction of deformities.

PROCEDURE

The purpose of this brief paper is to emphasize the need for excision of the infected, sclerotic portion of the bone, to describe a method for dealing with some of the resulting bone cavities, and to point out the value of amputation and of resection of certain bones in the treatment of chronic osteomyelitis. At the same time it is stressed that, along with local treatment of the disease, every effort must be made to improve the patient's general condition and his resistance to infection. Energetic and persistent attempts to correct deficiencies of protein, fluid, hemoglobin, electrolytes, and vitamins should be made. As pointed out by Penberthy and others "a debilitated patient is a good host for bacteria."

During the operation for the cure of chronic osteomyelitis the excision of the infected sclerotic bone presents no great difficulty except in cases in which complete removal would so weaken the bone that a fracture is likely. A more limited resection may have to be accepted at the first operation in the knowledge that a further resection will subsequently be required if there is to be no recurrence of the osteomyelitis and if a pathologic fracture

is to be avoided. Incidentally, if such a fracture does occur, union may be expected following immobilization. Usually, the clearing out of infected bone proceeds till apparently normal, bleeding cancellous bone is exposed all round. In all cases a special search should be made for tracks leading down the shaft. In some cases there may be little demarcation between infected cancellous bone and dirty-looking granulation tissue; but it is not necessary to distinguish between them at operation. Both require removal. If for some reason clearance of the infected tissues and bone appears to be incomplete at the end of the operation postoperative irrigation of the wound with monacrin, as described by Turnbull in 1944, or other suitable solution is indicated. For providing dependent drains and for irrigation of these wounds lucite, mentioned by Dennis in 1943, and similar materials offer certain advantages.

If the epiphyseal plate is seen at operation it is respected, but in the presence of chronic infection it may be difficult to define. When the periosteum has been raised by abscesses its removal is imperative to allow their drainage, but care must be taken not to denude the retained bone of its periosteum. It is interesting to note that even when most of the shaft of the femur is involved by the chronic osteomyelitic processes the region of the linea aspera usually escapes. This fact is undoubtedly due to the firm attachment of the periosteum in this region.

Whatever method of treatment is employed, postoperative immobilization of the limb in a splint or a plaster of paris cast is, of course, important.

The methods for dealing with the bone cavities of chronic osteomyelitis after the pus, sequestra, infected bone, and debris are removed include immediate and delayed split skin grafts to the cavity wall, as described by Quick in 1943. These methods also include filling the cavity with a muscle or fat graft or with cancellous bone chips followed there and then or later by covering with a pedicle graft, either obtained locally or from a distance. Incidentally, these pedicle grafts must be sufficiently extensive to be attached to tissues with normal vascularity well wide of the relatively avascular surrounding tissues. Such pedicle grafts from a distance are usually reserved for patients in whom other methods have failed.

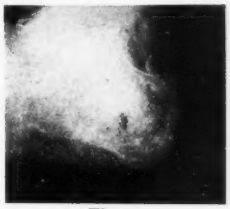


Fig. 4.

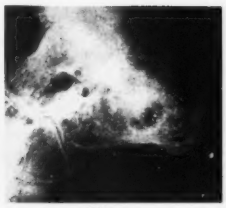


Fig. 5.

Fig. 4. Chronic osteomyelitis of the os calcis following the use of a Steinmann pin. One end of the tubular sequestrum may just be seen.

Fig. 5. A roentgenogram of the same os calcis as in Figure 4 taken some 3 months after sequestrectomy and saucerization followed by the application of a mold to the wound. The depression on the medial side of the os calcis was completely epithelialized and there has been no sign of activity in the 7 years since then.

Even with the various antibiotics the control of the infecting organisms may present many difficulties and, if not controlled, they may result in failure of all attempts at skin grafting. As on other occasions, the "take" of the graft may also be poor due to insufficient blood supply. Obliteration of the cavity by bone chips or by a graft of muscle or fat and covering with a pedicle graft may be eminently satisfactory especially in the treatment of localized chronic abscesses (Fig. 2); but, sometimes, the application of a roof over the cavity facilitates reactivation of the infection and little or nothing is gained by the operation.

Following operation on a localized chronic bone abscess (Brodie's) primary closure is desirable, for it should prevent the inevitable secondary infection which must follow an open wound. On the other hand, a single, localized, chronic bone abscess may become quiescent after treatment with chemotherapeutic agents and operation may sometimes be postponed indefinitely (Fig. 3).

Chronic osteomyelitis of the os calcis may follow an acute hematogenous infection, but more often it results from compound fractures or from infection around a Steinmann pin (Fig. 4) or Kirschner wire. Saucerization and the insertion of a mold, as mentioned later, will usually give good results (Fig. 5); but, if

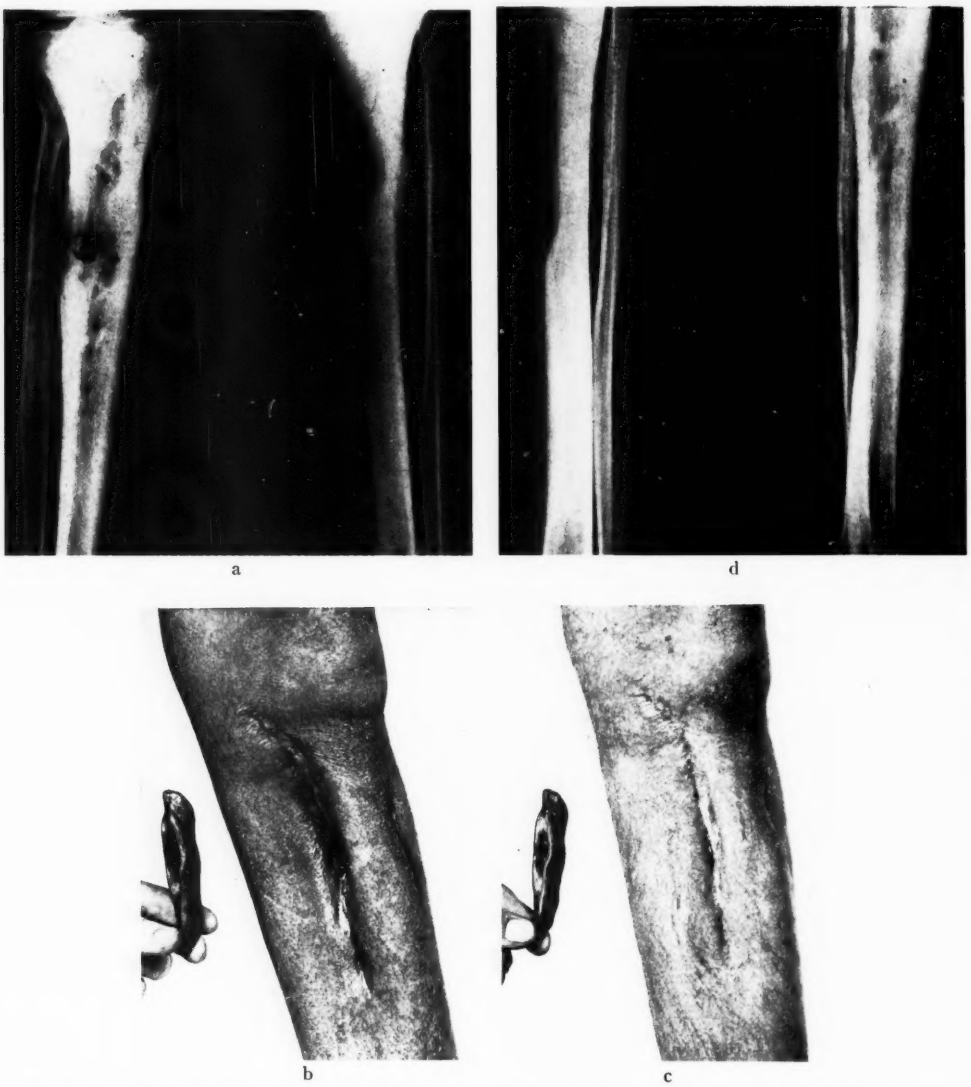


Fig. 6. a, Chronic osteomyelitis following acute hematogenous osteomyelitis. Roentgenogram of the upper two-thirds of the tibia and fibula showing the involvement of nearly half of the tibia and the presence of at least one sequestrum. b, Four weeks after saucerization of the affected portion of the bone and removal of the sequestrum. In this case a mold of dental impression compound was used. c, After a further month by which time the depression was firmly epithelialized. d, A roentgenogram 9 months after operation showing extent of bone removed.

the joint surfaces are destroyed, excision of the bone is indicated. After such excision a special shoe is necessary; but, with it, the functional result may be very satisfactory.

As pointed out by Butler in 1940, osteomyelitis of the pelvis runs a different course from infection of the long bones because of its anatomic structure. With its various centers

a

c

b

Fig. 7. a, Chronic osteomyelitis of the lower end of the tibia which developed following an injury to the leg but without a fracture. Various operative procedures including split skin grafting to the walls of the saucerized cavity had previously been tried. b, One month after saucerization and the application of the mold to the wound without skin grafting. Persistent infection in the recess in the lower angle of the wound delayed healing for a further 6 months. It will be seen from the shape of the mold that it had been considered inadvisable to lay the lower part of the wound wide open because of the proximity of the ankle joint. c, A roentgenogram 8 months after operation showing the extent of the bone removed.

of ossification, its many epiphyses, and the relatively small marrow cavity, widespread infection with destruction of the bone is rare. Sequestration and involucrum formation are not as common as in some bones. However, a chronic osteitis of the surrounding bone is almost invariable. Also, a focus of infection in the anterior inferior iliac spine is very likely to spread into the hip joint. Chronic osteomyelitis of the pelvis presents various problems in treatment for: the infected bone may be difficult to expose because of the thick scar tissue lining the sinuses, especially the frequently occurring posteriorly placed ones; general toxemia is more likely to be severe, and septicemia is more likely suddenly to arise than in patients with infections in other bones; the direct spread of the infection may give rise to a pelvic or psoas abscess; and often it may be practically impossible to expose and drain all the infected bone. There are many possible sites for the initial infection in the pelvis, but the ilium is most frequently attacked. On the rare occasion when the infection is limited to the ilium near the crest, the

a

Fig. 8. b

Fig. 9.

Fig. 8. a, Chronic osteomyelitis of the lower end of the radius and septic arthritis of the wrist joint due to an old gunshot wound. b, One month after saucerization and the application of a mold. As a result of the original injury and the subsequent fibrosis, there was considerable fixation of the extensor tendons which required attention later.

Fig. 9. Chronic osteomyelitis of the midshaft of the femur. All the obviously affected bone has been removed. The wound was irrigated with penicillin solution using the deepest mold shown in Figure 10. In the 7 years since then a further operation for drainage has been performed.

whole of the infected bone may be ablated without affecting the rigidity of the pelvis as a whole. It is to be noted that curettage and filling with bone chips of a localized bone infection of the pelvis, especially in the sacroiliac region, are unlikely to succeed.

SAUCERIZATION WITH INSERTION OF A MOLD

When a bone cavity is saucerized and allowed to heal with the formation of granulation tissue the development of an involucrum may form a new roof over the infection which persists in the depths of the granulation tissue. In order to prevent this formation of involucrum (which is frequently far from advantageous) and in order to avoid the problems associated with the application of split skin grafts to the cavity walls, it is suggested that a mold be maintained in the wound during its healing (Figs. 6 and 7). The mold of a nonirritating and sterilizable material (e.g. glazed and baked clay) (Fig. 8) is held in the wound with sufficient pressure to prevent the overgrowth of exuberant granulation tissue. One advantage of the mold is that it may be removed as required for its own cleansing and for the toilet of the wound. Thus, with the ingrowth of epithelium from the wound's edges the surface of the cavity heals by second intention leaving a permanent, noninflamed, epithelium lined depression. In other words, the cavity or depression is accepted as inevitable once all the infected bone and bone marrow have been removed, and an attempt is then made to encourage epithelium to grow in over its surface.

The mold should not be so tight as to interfere with drainage or with the ingrowth of epithelium; but, at the same time, it should

yet be big enough to keep the cavity open. It is often found necessary to apply firm pressure to the mold to try to prevent its extrusion. However, if it is partly extruded this need not be of any significance.

Plugs of vaseline gauze are not suitable for use in place of the rigid mold. If sufficient pressure is applied to make the vaseline gauze firm and to exert pressure on the walls of the cavity it acts as a plug which interferes with drainage. Also, there is no capillary effect with gauze covered with vaseline. If a dressing is to be applied to these wounds it appears that glass cloth is preferable to vaselined gauze, as Wilson has pointed out.

This method of saucerization followed by insertion of a mold into the wound might be called "healing with persistent cavitation," and is especially suitable for use in recurrent cases of chronic osteomyelitis of the shafts of the superficial bones such as the tibia, radius, and ulna; and it has been used in 22 such cases during the past 9 years. In all but 1 case of osteomyelitis of the lower end of the tibia and 1 case of infection of the greater trochanter of the femur, its use has been associated with the desired result of healing of the cavity and with the absence of any recurrence of detectable inflammation since then. In these 2 cases the method probably failed because of insufficient saucerization of the cavity, that is, it was left too deep relative to its opening. In the case of failure to eradicate the infection, or rather to cause the infection to become quiescent, in the tibia, there was the suggestion from the ward nurse that the patient was interfering with the wound.

On the other hand, this method is less satisfactory when the infection is situated toward the articular ends of the bones. It is also unsatisfactory in the deeper parts of the femur, humerus, and other deeply placed bones. In the latter, better results are obtained by providing proper and dependent drainage after the removal of all the infected bone (Fig. 9) and then irrigating the wound frequently. Such free drainage of a deeply placed infection may be attained by flattened and irregular, tubular molds, as shown in Figure 10.

If saucerization is not possible a secondary opening may be made in the opposite side of the bone to allow dependent drainage or to change the site of the sinus, if such exists. For instance, this was carried out in a man of 23 who had developed a chronic osteomyelitis of the lower end of the tibia following a compound fracture some years previously. The sinus was present behind the lateral malleolus and led down to the infected bone in the lower end of the tibia (Fig. 11). The fibula had been fractured but was not infected. At operation, a secondary opening was made over the medial aspect of the lower end of the tibia, the diseased bone removed, and the lateral sinus excised. In the following 2 months, the medial wound was kept open till the lateral sinus healed. Then, the medial wound was allowed to close. If a short sinus had persisted on the medial side of the tibia it would have been easier to deal with.

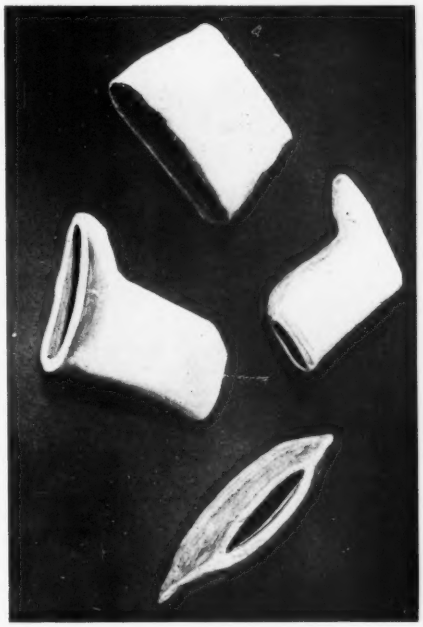
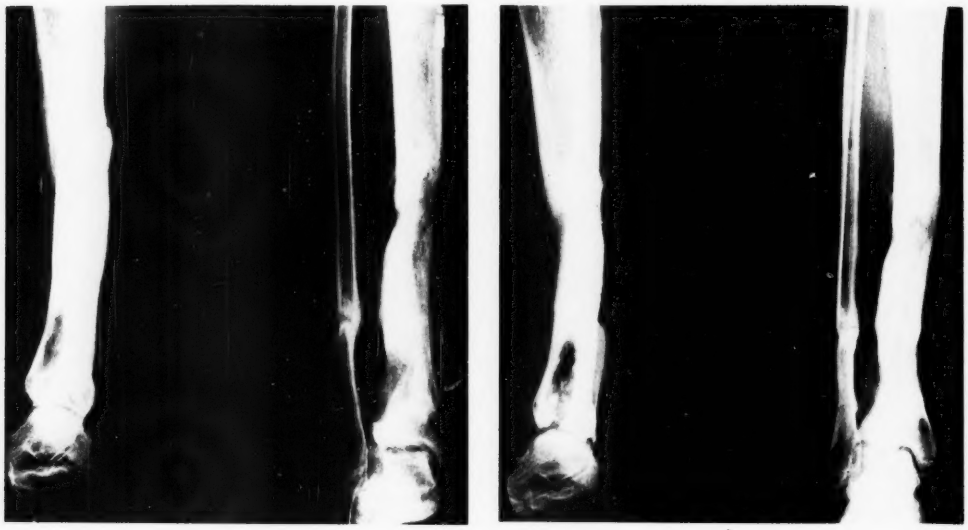


Fig. 10. Molds which have been used to drain or irrigate deeply placed areas of chronic osteomyelitis in the femur.

Various materials have been tried for the molds but the baked and glazed clay is preferred. It was found that dental composition had the disadvantages of being difficult to disinfect and of being likely to fragment. Acrylic



a b

Fig. 11. a, Chronic osteomyelitis of the lower end of the tibia following a compound fracture. The discharging sinuses were situated on the lateral aspect of the leg although the fibula was not infected. By draining the medial aspect of the lower end of the tibia healing was obtained in less than 4 months. b, Thirteen months later. There had been no recurrence of infection. Persistence of the excavation from side to side through lower end of tibia is seen.

material was an improvement, but more costly. After molding, the clay is baked and glazed, and it then presents no difficulty in sterilizing by chemical methods or by boiling as long as it is not plunged into hot water.

After a cavity in the lower limb has become epithelialized the mold is retained in place with slight pressure for a few weeks to prevent subepithelial edema.

In some cases the partial extrusion of the mold has necessitated the preparation of another, but slightly smaller, mold. In these cases healing has still been satisfactory.

Other valuable methods of dealing with persistent and recurrent chronic osteomyelitis are amputation of the limb and excision of the affected bone.

AMPUTATION

Amputation is indicated in the patient who already has undergone years of invalidity and who has similar prospects for the future. Repeated sequestrectomies and drainage of chronic osteomyelitic cavities may cause only temporary remissions without any great possibility of clearing up the infection permanently. Cases seen at intervals should be carefully reviewed, and the fact that the patient is at least a semi-invalid should not be ignored.

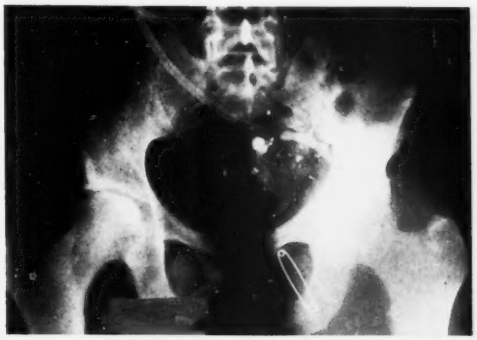
Amputation is also indicated in patients whose limb, because of incurable deformity or intractable pain, will always be useless. Occasionally, amputation is required as a life-saving measure. Amputation will often be indicated when such lesions as suppurative arthritis, pathologic dislocations, nerve lesions, and secondary hemorrhages complicate an intractable chronic osteomyelitis (Fig. 12). The onset of malignancy in the sinuses of chronic osteomyelitis has been recorded by Devas and is another, albeit unusual, indication for amputation. However, apart from these clear cut indications there are cases in which it should be apparent that amputation has much to offer and would result in less suffering and less disability.

A lesion of the tibia is more amenable to treatment than that of the femur and if amputation for chronic osteomyelitis is eventually

Fig. 12.

Fig. 12. Chronic osteomyelitis following a compound fracture. Because of the persistent pain, the destruction of the lateral side of the knee joint and the failure of repeated operations to clear up the infection a decision had been made to amputate the leg. The wisdom of this was unchallenged when a brisk secondary hemorrhage occurred. The postoperative course was very satisfactory, and 2 months later he was able to commence work as a lift driver.

Fig. 13. a, Multiple wounds of the left side of the pelvis due to bomb fragments led to an acute infection which became established. Attempts to eliminate the infection by irrigation and drainage were unsuccessful and a suppurative arthritis of the hip joint developed. b, After a further 6 months his condition was rapidly deteriorating, and the hip joint was stiff and painful and had been destroyed by the infection. The spread of the infection to the inner aspect of the pelvic bone is indicated. c, Four months after the amputation through the upper end of the femur. It will be noted that the infection on the inner aspect of the pelvis has now subsided.



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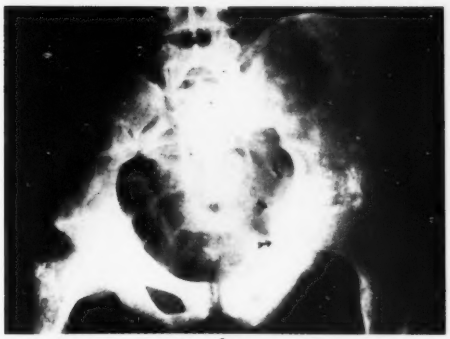

b

c

Fig. 13.

necessary it is more likely to be high in the thigh than lower down the thigh or below the knee. Even so, the patient will often be much better off without his leg (and infection) rather than spending years incapacitated by pain and toxemia. Even if the leg were saved it may only be a poor limb which would continue to give trouble, and which would be much less useful than an artificial limb. Amputation abolishes the toxemia and the ever present risk of metastatic infection of other bones or viscera and even of septicemia.

As Perkins pointed out in 1946, with the exhibition of penicillin it is usually safe to do a

Fig. 14. Localized chronic osteomyelitis of the shaft of the fibula which was treated by excision of three quarters of the bone.

definitive amputation at the site of election even though there is infection lower in the limb.

In the upper limb there is a much smaller place for amputation, for, in the absence of weight bearing, the disease is much less likely to be intractable.

The invaluable position of amputation in treatment of chronic osteomyelitis was brought home by 2 similar cases of chronic osteomyelitis of the sacroiliac region of the pelvis under my care at the same time.

In the first the inflammation had apparently become quiescent and eventually there was no pyrexia, sinuses, leucocytosis, pain or other signs of activity; and yet 4 months after weight bearing commenced death ensued due to a flare-up of the infection and to septicemia. This was despite what was considered to be an adequate chemotherapeutic cover at the time weight bearing was started.

In the second case it was believed that a similar sequence was very likely if it were ever possible to reach a stage at which there was no evidence of active inflammation. In this case the hip joint was stiff and painful and would never move again (Fig. 13); and there had been a steady deterioration in his general condition rather than any improvement. In addition, he had suffered a complete sciatic nerve lesion at the time of the wounding, and after 14 months there was no evidence of any recovery.

Because of the grave anesthetic risk and the difficulties that would have been encountered if a disarticulation at the hip joint had been attempted through the mass of the scar tissue, an amputation was carried out just below the trochanters. This operation was associated with little general upset and thereafter his condition rapidly improved.

Although the inflammatory foci were left in situ and although the amount of movement of the leg had been minimal and there had been no weight bearing, the removal of the leg was followed by a rapid subsidence of the inflammation, and in the 7 years since then there has been no recurrence. From being mentally confused for some weeks he was able to start training as a commercial artist 4 weeks after the amputation. Because of the fear that weight bearing might cause an exacerbation of inflammation or even a septicemia, as in the patient quoted previously, this man has been advised not to attempt to wear a prosthesis; and he is very happy with his crutches.

The alternative to amputation below the trochanters in this patient was perhaps a hindquarter amputation. In view of his extremely poor general condition this was, however, quite out of the question as an emergency procedure. Nevertheless, if the inflammation had persisted after the high amputation, such a radical operation would have required consideration.

RESECTION OF THE AFFECTED BONE IN WHOLE OR IN PART

The bone which most often lends itself to successful excision for chronic osteomyelitis is the fibula (Fig. 14). Less often, the whole or part of the clavicle, small bones of the hands and feet, ribs, and perhaps the radius or ulna may be resected. The results in these cases are very satisfactory and it is to be regretted that such excision is not more widely appli-

able. After such excision first intention healing may occur.

If only portion of one of these bones is being removed it is best accomplished with a Gigli saw so long as the sclerotic bone around the affected area is avoided. In the case of the fibula both ends of the bone should be allowed to remain in situ if unaffected. Removal of the lateral malleolus leads to a valgus deformity of the ankle, while removal of the head of the bone may be associated with injury to the common peroneal nerve.

On the other hand, attempts to eradicate the infection in chronic osteomyelitis of one of the larger long bones by diaphysectomy are usually unsuccessful and lead to deformity.

CHRONIC INFECTION OF CARTILAGE

While discussing the treatment of chronic osteomyelitis the treatment of chronic infections of cartilages, such as the costal cartilages, should also be mentioned. If such a cartilage is denuded of its perichondrium and is infected, a persistent sinus and persistence of the infection will occur, as Maier has shown, and will only be eradicated by complete excision of the involved cartilage. Such infection may follow radical mastectomy, thoracotomy, and upper abdominal operations if the costal cartilages are injured and infected.

SUMMARY

A simple and effective method of treating chronic osteomyelitis in the more superficial parts of bones is proposed.

Amputation and resection of certain bones are of value in the treatment of some cases of chronic osteomyelitis.

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THE COMBINED ANTERIOR SURGICAL APPROACH TO CARCINOMA OF THE UPPER THORACIC ESOPHAGUS

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SINCE the report of Lewis in 1946 stating the advantages of an approach to malignant tumors of the upper esophagus from the right side of the thorax, considerable clinical evidence has accumulated to support this point of view. From the anatomic standpoint there is no doubt that the surgical exposure of the thoracic esophagus is better from the right than from the left side of the chest. The azygos vein is the only structure which impedes exposure on the right while the aortic arch presents a major obstacle on the left. Macmanus, Kent and Harbison, Harrison and Pickett, Mathewson and Cohn, Gaspar and Snyder, and others have presented convincing arguments based on extensive clinical experience which stress the value of the approach to the esophagus from the right.

Following the lead of Garlock and Sweet in 1948 numerous reports have demonstrated the feasibility of restoring esophagogastric continuity after resection of carcinomas of the upper fourth of the esophagus by bringing the mobilized stomach upward through the left thorax into the neck for anastomosis to the esophagus through a cervical incision. In 1950 one of us with Hanlon stressed the advantages of a simultaneous cervical and thoracic exposure of these difficult tumors so as to permit mobilization of the lesion by sharp dissection under direct vision (10). However, the technique used, like that described by Garlock, Sweet, and others, included a left posterolateral thoracotomy with transdiaphragmatic mobilization of the stomach.

In order to avoid damage to the left diaphragm and to facilitate gastric mobilization a separate abdominal incision has been employed by most of the advocates of the right thoracic approach to the esophagus, but this has usually necessitated changing the patient's position on the operating table. Furthermore, unless several changes in position are to be entertained, this operative plan requires that the abdominal phase of the procedure with mobilization of the stomach be carried out before the status of the esophageal lesion is known.

The technical plan which we believe at present to offer fewer disadvantages and to facilitate greatly the operative handling of carcinomas of the upper thoracic esophagus is, with minor modifications, identical with that described by Harrison and Pickett.

TECHNIQUE OF OPERATION

The patient is placed in recumbent position with the right side of the chest moderately elevated and the head turned to the left (Fig. 1A). The right side of the neck, the right hemithorax, and the upper abdomen are prepared and draped. A submammary anterior thoracotomy incision is placed on the right, pectoral muscles are divided, and the thorax is entered in the third intercostal space. The third and fourth costal cartilages are divided to provide maximal exposure. The apex of the lung is retracted downward, and the azygos vein is doubly ligated and divided. The mediastinal pleura overlying the esophagus is incised up to the apex of the thorax. The esophageal lesion is visualized and dissection is initiated to mobilize the esophagus and the tumor (Fig. 1B).

If the tumor lies at the thoracic inlet the dissection is facilitated by simultaneous cervical and thoracic exposures. However, if the esophageal lesion lies entirely within the thorax the abdominal phase of the procedure may be initiated by part of the surgical team.

An upper midline or paramedian abdominal incision is placed extending from umbilicus up to the left of the xiphoid cartilage and the

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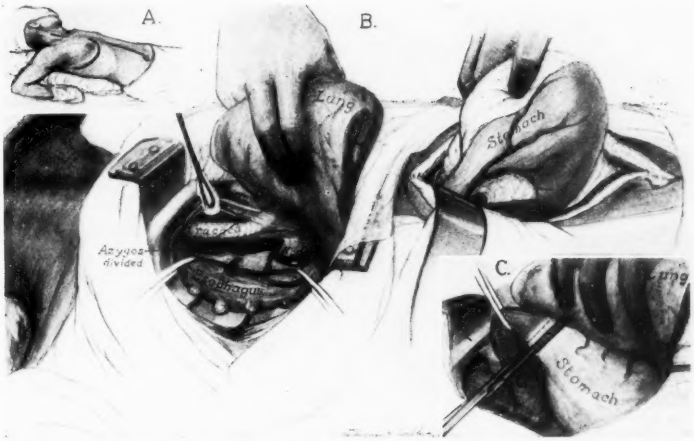

Fig. 1. Technique of operation. A, Position on table with sites of incisions used. B, Esophagus and tumor mobilized by thoracic operator while stomach is freed by abdominal team. C, Mobilized stomach delivered into right hemithorax prior to division of esophagogastric junction.

abdomen is inspected for metastases. An extensive mobilization of the stomach is then carried out which preserves only the right gastric and right gastroepiploic vessels and the vascular arches along the curvatures. The parietal peritoneum lateral to the duodenum is divided, the surgical cleavage plane is entered, and the duodenum and pancreas are mobilized freely to displace these structures toward the hiatus. The peritoneum at the esophageal hiatus is incised and the esophagus is freed from its attachments in this region. A Ramstedt pyloromyotomy is done before the stomach is drawn up into the right thorax.

After the dissection of the esophagus has been completed in the environs of the tumor in such a way that all enlarged nodes are to be resected with the esophagus, the lung is retracted anteriorly, and the thoracic operator carries the mediastinal pleural incision down to the diaphragm. The entire thoracic esophagus is then mobilized and esophageal arteries are ligated and divided.

The mobilized stomach is then drawn up into the right thorax through the hiatus. After ligation at the cardia the esophagus is divided and its proximal end covered with a segment of rubber drain. The distal end is inverted

Fig. 2. The fundus of the mobilized stomach is drawn up to the right apex. The cervical esophagus has been exposed through an incision in the right side of the neck, as described in the text.

Fig. 3. Gastric fundus has been drawn up into cervical wound for anastomosis to esophagus just below pharynx. Abdominal wound is closed by part of the team while the anastomosis is in progress.

Fig. 4.

Fig. 5.

Fig. 4. Case 1. Preoperative esophagogram; lateral view.
Fig. 5. Case 1. Roentgenogram of chest with barium swallow after esophagectomy and cervical esophagogastric anastomosis; oblique view.

into the stomach with two rows of interrupted silk sutures (Fig. 1C).

A cervical incision is now placed (assuming that this has not been necessitated earlier in the operation by the presence of an extremely high esophageal tumor) along the anterior border of the right sternomastoid muscle down to the suprasternal notch. The sternomastoid muscle and the carotid sheath are retracted laterally, the middle thyroid vein is divided, and the thyroid and trachea are gently retracted medially to expose the cervical esophagus. The latter is freed circumferentially from the pharynx down through the thoracic inlet to the plane of the mediastinal dissection (Fig. 2). The clavicle and first rib are not disturbed. The mobilized esophagus and the tumor are drawn up out of the chest into the cervical wound. The fundus of the stomach is then brought up to the apex of the chest behind the hilum of the lung and is passed dorsal and medial to the right subclavian and carotid arteries. By means of an Allis clamp passed downward from the cervical incision between the trachea and the carotid sheath the apex of the gastric fundus is drawn upward through the thoracic inlet and forward into the cervical wound. Manipulation of the stomach from above and below permits an adequate portion of the fundus to lie without tension in the cervical wound. This allows satisfactory anastomosis of the stomach to the esophagus just below the cricopharyngeus.

The esophagogastric anastomosis is carried out as previously described in detail by Scott and Hanlon. The placement of the posterior row, consisting of interrupted fine silk sutures, is facilitated by using the distal esophagus as a handle to expose the posterior esophageal wall immediately below the pharynx (Fig. 3). After these sutures are tied an incision is made through the posterior esophageal wall and through the wall of the adjacent stomach. The posterior row of the internal layer of the anastomosis is then placed so as to approxi-

Fig. 6. Case 2. Preoperative esophagogram; anteroposterior view.

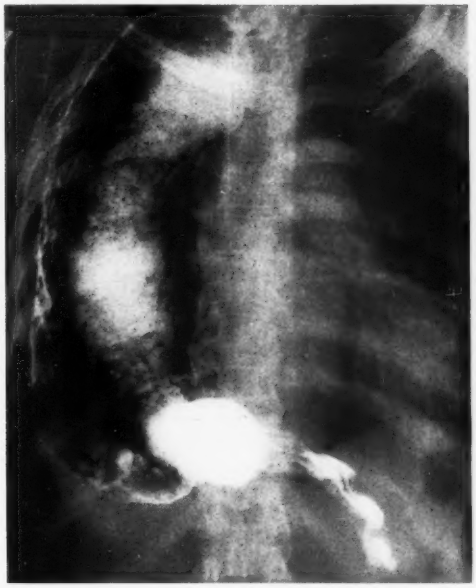

Fig. 7. Case 2. Postoperative roentgenogram of chest with barium swallow; anteroposterior view.

ate the full thickness of the esophageal wall to that of the stomach by interrupted inverting sutures of fine silk with the knots tied inside the lumen. The anterior esophageal wall is then divided, the entire length of hypopharyngeal esophagus with the tumor is removed, and the internal and external layers of the anastomosis are completed anteriorly. A small nasal catheter is passed through the anastomosis into the intrathoracic portion of stomach to maintain gastric decompression during postoperative period. The cervical wound is then closed in layers with fine silk.

While the cervical wound is being closed the stomach is anchored to the mediastinum and posterior parietal pleura of the right hemithorax with multiple interrupted sutures. The lung is re-expanded by the anesthetist, a large Pezzer catheter is led out through a stab wound in the fifth intercostal space in the midaxillary line for water sealed drainage, and the thoracotomy wound is closed in layers with interrupted silk sutures.

Before closing the abdominal wound the relations of the antrum of the stomach to the esophageal hiatus are assessed and if the fit seems to be too snug the hiatus may be enlarged by dividing the right diaphragmatic crus. The peritoneum at the periphery of the hiatus is tacked to the antrum with interrupted sutures. The abdominal wound is then closed in layers.

CASE REPORTS

CASE 1. L. O., a 68 year old white female, was admitted to the Vanderbilt University Hospital on March 24, 1953, with a 4 months' history of progressive dysphagia accompanied by substernal pain, frequent regurgitation, and occasionally aspiration of liquids. There was weight loss of undetermined amount. Physical examination revealed an emaciated, dehydrated, elderly female who weighed 85 pounds but otherwise was in good general condition. There was no cervical lymphadenopathy nor was the liver palpable. Laboratory studies were within normal limits and an x-ray film of the heart and lungs revealed no abnormalities.

An esophagogram (Fig. 4) demonstrated a 4 centimeter area of constriction with mucosal destruction 3 centimeters above the superior surface of the aortic arch. Esophagoscopy demonstrated a fungating mass obstructing the esophageal lumen at the level of radiologic constriction. A biopsy of this

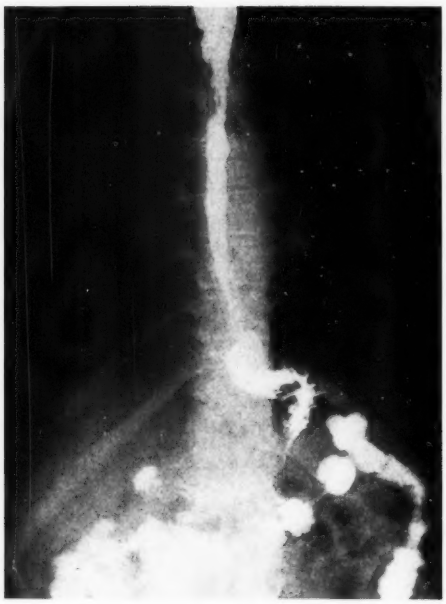

Fig. 8. Case 3. Preoperative esophagogram; anteroposterior view.

Fig. 9. Case 3. Roentgenogram of chest with barium swallow in early postoperative period; anteroposterior view.

lesion revealed a well differentiated squamous cell carcinoma.

On March 30, 1953 under endotracheal gas oxygen ether anesthesia a two team combined cervicothoracoabdominal esophagectomy with cervical esophagogastrostomy was performed as described previously. A pyloromyotomy was also carried out. The resection was a palliative one in that the tumor was densely adherent to the trachea and no doubt carcinoma was left at this site. Furthermore, microscopically carcinoma extended through the muscle layer into the surrounding connective tissue. The architecture of one lymph node was completely destroyed by tumor.

The postoperative course was entirely uncomplicated and the patient was discharged on the fourteenth postoperative day, taking a regular diet in 6 feedings without regurgitation, dysphagia, or distress. A gastrointestinal series (Fig. 5) prior to discharge revealed the anastomosis to be at the level of the sternoclavicular joint and there was no delay in passage of the barium from the esophagus into the stomach and on into the small intestine. In the 2 months since discharge the patient has taken regular diet without any difficulty and has gained 5 pounds.

Case 2. K. P., a 51 year old colored female, was admitted to the Vanderbilt University Hospital on May 1, 1953 with a history of progressive dysphagia accompanied by substernal burning pain of 5 weeks' duration. There was a 9 pound weight loss during her illness. Physical examination revealed a thin, well hydrated female with minimal evidence of weight loss. There was no cervical lymphadenopathy and no gross stigmas of inoperability. Laboratory studies demonstrated no anemia, hypoproteinemia, or electrolyte imbalance.

An esophagogram (Fig. 6) revealed a circumferential narrowing of the esophagus just below the aortic arch. Esophagoscopy demonstrated a fungating lesion 28 centimeters below the level of the upper teeth. On biopsy this lesion proved to be a well differentiated squamous cell carcinoma. Bronchoscopy revealed no invasion of the trachea.

On May 6, 1953 a two team combined cervicothoracoabdominal esophagectomy with cervical esophagogastrostomy was performed under endotracheal anesthesia. Although the tumor was located in the second fourth of the esophagus large paraesophageal nodes were present up to within 4 to 6 centimeters of the thoracic inlet, necessitating a cervical anastomosis. A pyloromyotomy was also performed. At pathologic examination of the specimen the tumor occupied two-fifths of the length of the esophagus, and there was a 5 centimeter margin of normal mucosa proximal to the lesion. Microscopically this was an anaplastic squamous cell carcinoma and all paraesophageal lymph nodes contained metastases. Forty-eight hours postoperatively a tracheotomy was done because of ineffective expectoration of bronchial secretions. The patient

as discharged on the fifteenth postoperative day on regular diet. A gastrointestinal series (Fig. 7) prior discharge revealed no delay in emptying of the omach. In the month since leaving the hospital he patient has eaten regular diet without difficulty nd weight is being maintained.

CASE 3. S. B. E., a 56 year old white male, was dmitted to the Thayer Veterans Administration lospital on November 22, 1952 with a 4 months' istory of progressive dysphagia. At the time of adission he could swallow only liquids. There was a eight loss of 10 pounds in the preceding period of months. Past history was noncontributory with e exception of closure of a perforated duodenal lcer in 1936.

Physical examination revealed a thin, white male no acute distress. The heart and lungs were noral. There was no cervical lymphadenopathy nor as the liver palpable.

Laboratory studies showed blood count and rinalysis to be within normal limits. Liver function udies were normal. X-ray examination of the art and lungs revealed no abnormalities. An ophagogram (Fig. 8) revealed a filling defect in e esophagus just above the level of the aortic ch, with partial esophageal obstruction in this gion. The remainder of the gastrointestinal series as within normal limits.

On December 1, 1952 esophagoscopy was performed, and an ulcerative lesion was noted at a point centimeters distal to the incisor teeth. The lumen the esophagus was partially obstructed at this oint. A biopsy of the ulcerative lesion revealed an naplastic squamous cell carcinoma of the esophagus. Bronchoscopy was negative. After a period of preoperative preparation a combined cervicothoracoabdominal esophagectomy with cervical esophagogastrostomy was performed. There was no evidence of direct extension into the adjacent structures nd no gross evidence of lymph node involvement in the mediastinum. A pyloromyotomy was performed prior to delivery of the stomach into the chest.

Pathologic examination of the specimen confirmed the biopsy diagnosis and revealed the presence of one lymph node which was involved with metastatic tumor.

In the postoperative period the patient developed a wound infection with subsequent postoperative herniation in the abdominal wound. There was a transitory diarrhea which required parenteral feedings and a graduated return to oral alimentation. A gastrointestinal series prior to discharge showed a satisfactory esophagogastrostomy and no delay in emptying of the stomach (Fig. 9). Five months following operation the patient returned complaining of some difficulty in swallowing. Esophagoscopy performed at this time revealed a slight narrowing of the esophageal orifice. There was no evidence of the presence of recurrent tumor, and currently the patient is responding favorably to esophageal dilatation.

COMMENT

The operative plan which has been detailed is advantageous in the surgical management of carcinoma at all but the lowest levels of the thoracic esophagus. We agree with Harrison and Pickett that lesions at or just above the diaphragm which may invade that structure are best dealt with by the conventional left thoracic approach. As pointed out by these authors the anterior, triple exposure approach to tumors of the upper and midthoracic esophagus with cervical esophagogastric anastomosis permits easier and more direct access to the involved area of esophagus, avoids the handicap of the aortic arch, and obviates the tendency to skimp on the length of esophagus to be resected. The technical difficulties and risk of high intrathoracic esophagogastric anastomosis are replaced by the easier, more accurate anastomosis in the cervical wound. Diaphragmatic function is preserved and, as Macmanus has emphasized, postoperative pulmonary complications are reduced.

In addition to these factors we believe that the anterior approach is less hazardous for the patient in that respiratory acidosis is probably less apt to be incurred in thoracic operations performed with the patient in supine position. Furthermore, since the patient's position on the operating table does not have to be altered during the procedure the danger of shock which may be associated with change in the position of the anesthetized patient is avoided.

Another advantage for both patient and the surgical team is that operating time may be reduced considerably by overlapping the operative procedures and the use of the two team principle.

It should be emphasized that excellent exposure of the thoracic esophagus is obtained through a widely opened anterior thoracotomy incision on the right. This is especially apparent in dealing with lesions above the level of the aortic arch. Exposure of esophageal tumors located at or just below the hilum of the lung necessitates careful retraction of the lung anteriorly, but mobilization of lesions at this level can be done quite adequately with this approach.

A tracheotomy, either at the completion of the operative procedure as in Case 3 or in the early postoperative period (Case 2), is often of considerable value in the management of patients with esophageal resection as has been stressed by Reynolds and his associates. Especially is this so with a high intracervical anastomosis and the additional factor of edema around the larynx secondary to the local operative trauma. We believe pyloromyotomy of the simple Ramstedt type to be a distinct adjunct in the successful use of the mobilized stomach to replace the thoracic esophagus. Since the vagus innervation of the stomach is interrupted by resection of the esophagus and mobilization of the stomach, gastric stasis may be a problem postoperatively unless this simple maneuver is carried out.

We are not yet prepared to accept the totally pessimistic point of view concerning high esophageal cancer recently presented by Ravitch and his colleagues although without question the surgical record thus far in the salvage of patients with these difficult lesions is meager indeed. The procedure under discussion is advanced as a means of improving the technical management of cancer of the middle and upper thoracic esophagus based on resection of the lesion, the entire thoracic esophagus, and paraesophageal nodes in a manner as radical as is permitted by the anatomic relations of the structures involved with restoration of deglutition and satisfactory oral alimentation in an effective and safe fashion. Since a more radical removal of esophagus and paraesophageal nodes is accomplished, this plan should give a better chance for complete extirpation of the tumor than does a less extensive resection. On the basis of the limited clinical experience which we have had with its use we can only state at present that the palliation provided by the procedure is quite satisfactory.

SUMMARY

A surgical approach to the problem of carcinoma of the upper thoracic esophagus involving the use of the supine position with anterior exposures through combined cervical, right thoracic, and abdominal incisions is discussed. The technique of operation is described in detail and illustrative cases are presented. The use of this plan in the technical management of carcinomas at all but the lowest levels of the thoracic esophagus is advocated and its many advantages are enumerated.

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ELECTROPOTENTIAL CHANGES IN THE ISOLATED MAMMALIAN URINARY BLADDER

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IN EARLIER reports from these laboratories (1, 3–6) electromyograms obtained from both normal and pathologic human urinary bladders have been described, together with alterations in intravesical pressure accompanying bioelectric activity. The present study was undertaken in an attempt to gain further insight into the fundamental nature and origin of the characteristic potential shifts associated with vesical activity, utilizing excised bladders from a variety of mammalian forms.

METHODS

Animals used in all experiments were sacrificed by means of a blow on the head in order to eliminate the possible effects of anesthetics. The bladder was quickly dissected, including approximately 1 centimeter of each ureter as well as of the urethra. The organ was then suspended under slight (1 gm.) tension in a bath of Sollman's solution at 38 degrees C. Oxygen was bubbled through this solution prior to its admission to the tissue chamber (100 c.c. capacity). Fine silver wire electrodes were attached at the fundus (dome) of the bladder and to the musculature just above the entrance of the ureters. Electropotential changes were recorded by means of a Grass electroencephalograph, suitably filtered.

Under these conditions, it was found that bioelectric currents were generated because of the very slight agitation produced by the passage of the solution through the bath. It was, therefore, necessary to arrest the flow of solution through the tissue chamber while records were being made. Hence, recording periods alternated with intervals during which the preparations were washed with the oxygenated fluid.

RESULTS

Spontaneous electropotential shifts occurred in the excised bladders of all the species studied: dog (3), cat (5), rabbit (3), guinea pig (5), and rat (60). Moreover, these electromyograms were indistinguishable in contour from those recorded from normal, unanesthetized human subjects (Fig. 1). As a rule, atypical activity indicative of hyperirritability was observed during the first few minutes of an experiment, due presumably to the trauma incident to the excision of the tissue.

All of the wave-forms seen in recordings from the human bladder were, on occasion, present: specifically those which we designated as "a", "A", and "B" waves (1, 6). This circumstance suggested the conclusion that the electropotential shifts recorded in the human bladder are solely of vesical origin, and that the bioelectric phenomena are not dependent upon central stimulation.

Because electromyograms secured from the bladder of the rat were indistinguishable from those exhibited by the human bladder as well as those of other mammalian forms, the rat bladder was employed in all further observations on the entire excised organ.

In order to discover whether these electropotential changes were due to an inherent myogenicity or to excitation arising from autonomic elements within the vesical wall, the bladder preparations were treated with various sympathomimetic and parasympathomimetic drugs, as well as with blocking agents. Response to acetylcholine was striking, particularly when applied to quiescent, hypoactive bladders. Thus, in 18 instances typical shifts in potential were evoked after an average interval of 16.8 seconds from tissues which had previously shown little or

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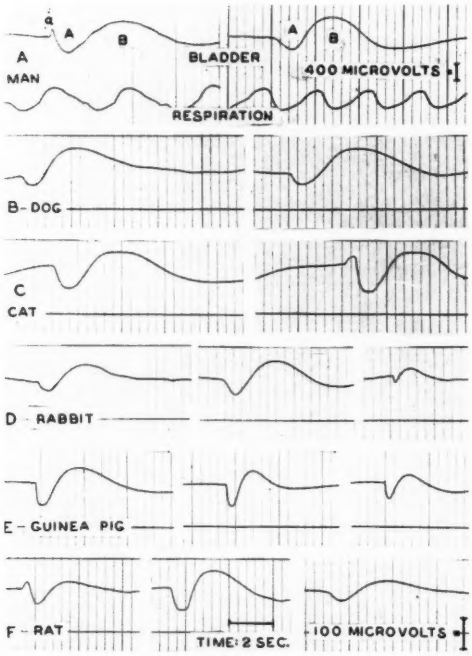

Fig. 1.

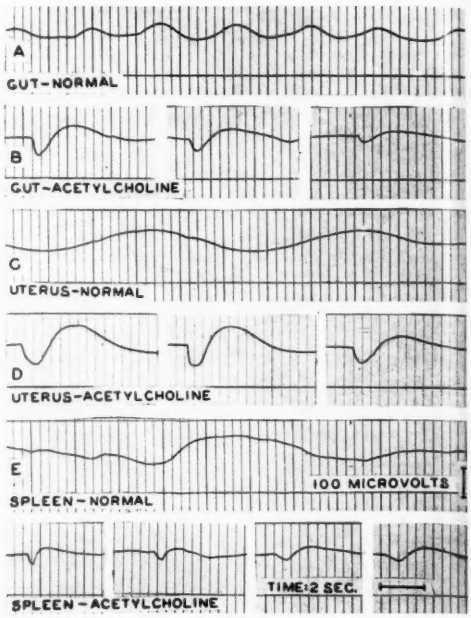

Fig. 2.

Fig. 1. Electromyograms secured during spontaneous activity in the urinary bladders of (A) man (*in situ*) and in the isolated bladders of a variety of mammalian species (B, C, D, E, F).

Fig. 2. Spontaneous electromyograms from isolated sections of rat intestine, uterus, and spleen, showing the effect of acetylcholine administration (1:250,000) on each. Note that differences are present in all of the control myograms, but that in each case exposure to acetylcholine resulted in an electropotential pattern very similar to that spontaneously produced by the urinary bladders of man and other mammalian types.

no spontaneous activity. So great were the voltages encountered that bioelectric potentials very frequently exceeded the scope of the recorder when amplification was so set as to register normal activity.

The response of the bladder to acetylcholine was then compared to that of other types of smooth muscle having autonomic innervation. Electromyograms were secured from sections of rat intestine, uterus, and spleen, and the response of each to acetylcholine in 1:250,000 dilution was noted. The results of these tests are exemplified by Figure 2. Note that the normal electromyograms from these organs in no way resembled those from the bladder, but that following exposure to acetylcholine, all of these tissues showed potential shifts identical in contour to those recorded from normal bladders. These results suggest that the bioelectric shifts spontaneously occurring in the bladder of man, as well as of other mammalian species, are in response to cholinergic nervous activity.

The reactions of rat bladders to the various drugs used in this phase of the study are tabulated in Table I. The table is based on average measurements of from 25 to 100 wave complexes following the administration of each of the drugs listed. For this reason, inspection of the table fails to give a true picture of the initial, and often dramatic effect of certain drugs on the electromyogram. For example, initial reaction to acetylcholine was usually of sufficient magnitude as to exceed the capacity of the oscillograph set for optimal normal recording. Hence these waves were not subject to measurement of potential. Conversely, at optimal sensitivity of the re-

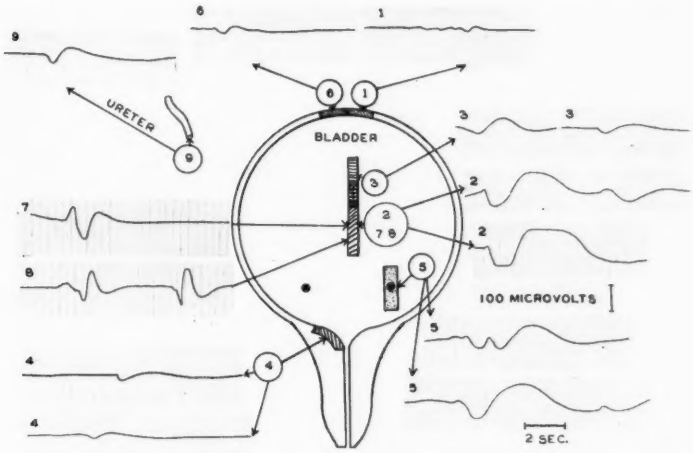

Fig. 3. Electromyograms obtained from isolated tissue samples secured from the human urinary bladder, showing the site of removal of each strip of tissue. Note that spontaneous bioelectric activity was greatest near the central portion of the organ, and much reduced in sections from the dome and vesical neck. All records were made at the same degree of amplification.

cocaine, adrenalin and banthine frequently halted bioelectric activity entirely, and, therefore, the degree of depression of electromotive force could not be determined. Atropine produced complete cessation of activity in all of the bladders tested, and the organ remained quiescent even after subsequent exposure to acetylcholine, except after prolonged (30 to 40 minutes) washing.

Adrenergic blockade by means of dibenzyline in a concentration of 1:500,000 evoked a prompt increase in bioelectric activity comparable to that of acetylcholine, and a definite increase could be detected at a concentration of 1:1,000,000.

It was observed that the cholinergic drugs appeared to increase the "A" potential in particular, even when the amplitudes of succeeding "B" waves approximated the normal.

From the reactions of the excised rat bladder to the chemical agents listed in Table I, indication was obtained of the parasympathetic origin of the spontaneous bioelectric shifts characteristic of the mammalian bladder including, by inference (from earlier studies), that of man.

If the bioelectric potentials observed were, indeed, initiated through parasympathetic neurones or nerve endings within the vesical musculature, it was considered that different portions of the viscus might well show differences in the potentials developed, depending on the relative concentration of such neurones or endings in the various portions of the organ. With the hope of clarifying this point, a series of 8 tissue samples was removed from the human bladder at operations in which cystostomy was necessary. These samples were from 1.2 to 1.6 grams in weight and were taken from the areas shown in Figure 3.

An examination of Figure 3 shows that there were marked differences in the magnitude of spontaneous bioelectric potentials exhibited by these tissues. Maximum potentials were seen in sections taken from centrally located sections and in the sample obtained at the entrance of the ureter. In contrast, the electromotive force generated by samples from the bladder dome and the vesical neck was much reduced. It is perhaps of interest that a section of the ureter, taken about 10 centimeters above the point of its entrance into the bladder yielded spontaneous electromyograms indistinguishable in contour from those exhibited by sections of the bladder wall. These observations provide further evidence that

TABLE I.—ELECTROPOTENTIAL RESPONSES OF EXCISED RAT BLADDERS TO AUTONOMIC DRUGS

Agent	Conc.	Freq. of wave (min.)	Duration of wave (sec.)	Duration "A" phase (sec.)	Duration "B" phase (sec.)	EMF "A" phase (uV)	EMF "B" phase (uV)
Normal	.....	3.5	3.793	0.904	2.889	39.772	50.885
Parasympathomimetic							
Acetylcholine	1:250,000	6.8	4.237	0.989	3.248	52.798	61.680
Prostigmine	1:100,000	7.0	4.209	0.991	3.218	52.699	61.522
Physostigmine	1:100,000	6.1	4.221	0.988	3.233	54.122	63.226
Furmethide	1:30,000	5.0	4.008	0.888	3.120	50.727	61.214
Parasympatholytic							
Banthine	1:200,000	0.4	4.209	1.160	3.130	13.055	25.661
Atropine	1:100,000	Complete suppression					
Sympathomimetic							
Adrenalin	1:100,000	1.2	4.374	1.170	3.204	18.000	21.220
Sympatholytic							
Regitine	1:100,000	4.8	3.825	0.894	2.931	50.888	61.521
Dibenzyline	1:500,000	7.1	4.208	0.991	3.217	53.878	64.422

the electromyograms which we have obtained from patients in the clinic do, in fact, represent true records of bioelectric activity within the bladder itself, and that there are differences in the magnitude of electropotentials generated by the musculature in various portions of the organ.

DISCUSSION

Although the characteristic electropotential pattern seen in clinical recordings (1, 4, 5, 6) may be considered to represent bioelectric activity originating in the bladder on a variety of evidence (6), such evidence has to date been of an indirect nature. Recently, Slater has recorded bladder potentials from the human subject by means of needle electrodes thrust into the wall of the viscus during cystoscopy. By this method, he has confirmed our observations in regard to the characteristic contour of the wave form as recorded by the oscillograph. However, the possibility has remained that potentials emanating from other viscera, or generated through movement of the electrodes might introduce artefact into the clinical record.

The observations described in the present report have clearly shown that records secured from the excised bladders of 5 mammalian species as well as from isolated portions of the human bladder produce electromyographic records which are indistinguishable in form from those secured from the intact bladder of the normal individual. It has been concluded, therefore, that the electromyograms which we have obtained from the human subject by means of placing transurethral electrodes in contact with the bladder wall are true representations of bioelectric activity within the bladder itself.

The results of the studies involving the use of drugs having an autonomic stimulatory or blocking action have been interpreted as evidence that the typical spontaneous electromyogram exhibited by the excised bladder is the result of smooth muscle response to stimulation by parasympathetic neurones or endings within the viscus. The effects of acetylcholine administration on the electromyograms of a variety of excised viscera (gut, uterus, spleen) tend to confirm this opinion.

In this connection, it is of interest that Swenson has reported that autonomic neurones within the bladder musculature are most numerous adjacent to the entrance of the ureters, diminishing toward the midline, and particularly toward the fundus and urethra—a finding entirely in keeping with the results described in our experiments with tissue samples from various portions of the human bladder. Campbell has reached a conclusion similar to our own in his studies of megaloureter, attributing this condition of atonicity to "subnormal parasympathetic nerve function." He further reports a "striking reduction in parasympathetic ganglion cells in the bladder wall musculature . . ." in instances of congenital megaloureter.

In view of this fact, one may consider the characteristic electromyogram typical of the

urinary bladder, whether obtained *in situ* from the human subject, or in isolated preparations, as representing response of the vesical musculature to parasympathetic bombardment. Hence, abnormalities in the cystoelectromyogram obtained in clinical practice may be interpreted as due either to interferences in normal innervation or to the response of a diseased musculature to parasympathetic bombardment.

SUMMARY

Electromyograms obtained from the isolated bladders of dogs, cats, rabbits, guinea pigs, and rats are indistinguishable in contour and general characteristics from those which are secured *in situ* from the normal human bladder.

Evidence from experiments involving the exposure of excised mammalian bladders to adrenergic and cholinergic agents, as well as blocking substances, is interpreted as indicating that the spontaneous bioelectric shifts observed are of the nature of responses to cholinergic, and therefore parasympathetic action.

Isolated sections from various portions of the human urinary bladder exhibited differences in the magnitude of bioelectric potentials which have been interpreted in terms of autonomic innervation.

It is suggested that the spontaneous and characteristic electromyogram of the mammalian urinary bladder, including that of man, is the result of smooth muscle response to parasympathetic bombardment.

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PRECIPITATING FACTORS IN VENOUS THROMBOSIS

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IN THIS article, our attempts to evaluate the current theories on the etiology of bland (noninfective) venous thrombosis are presented in a summarized form. Our approach to the problem has differed from that of previous investigators in that the criteria for the diagnosis of the disease have been pathologic rather than clinical. We have insisted on the actual demonstration of a thrombus at autopsy and have not, like others, accepted the signs and symptoms as a reliable index. And in this we have been influenced, not only by our own experience (8, 9), but by the reports of certain observers who, like Gage, state that "the clinical diagnosis of intravenous clotting is extremely difficult to make."

In our evaluations, then, complete dependence has been placed on the pathologic findings and, specifically, on the presence or absence of thrombi in the veins of the lower extremities as proved by dissection of these vessels. Dissections of this type have been done on 165 fatalities among middle aged or elderly patients in our hospital to date, and 72 of these, or 44 per cent, harbored definite thrombi. The technique of dissection has been described elsewhere (8), but in brief it consisted in the removal and examination of the veins, on each side, from the lower end of the inferior vena cava to the posterior tibial vein at the level of the internal malleolus. After the pathologic findings had been noted and confirmed by microscopic study, they were compared with the appropriate clinical and biochemical data obtained during life. To avoid bias, we have made it a firm rule that the antemortem findings were not to be revealed to the autopsy dissector until he had concluded his examination.

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The various theories that have been evaluated can be grouped into three categories:

The *theory of local injury* postulates that a lesion in the vein wall precedes, and causes, the initial thrombus deposition. We have assessed the validity of this statement by examining by complete serial section methods a number of tiny incipient thrombi observed in the course of our dissections.

The *theory of abnormal blood coagulability* has had, and still has, strong support in certain quarters. Among other things, it has been claimed that an increase in the blood fibrinogen or fibrinogen B level, a decrease in the blood antithrombin or alpha tocopherol level, a low fibrinolytic activity of the blood, or an excessive number of blood platelets, is the primary cause of thrombosis in veins. We have evaluated the importance of each of these blood components by determining their levels, serially, in critically ill patients during life, and in comparing the results of these tests with the pathologic findings in those patients who died and came to autopsy.

The *theory of venous stasis* has also been popular in the past. We have not made any direct measurements of blood flow in our patients, but have had to depend on indirect evidence and on certain general or local anatomic changes that might produce venous stasis and thus explain the deposition of a venous thrombus in a particular individual.

THE FACTOR OF LOCAL INJURY

As long ago as 1856, Brucke considered that alterations in the vein wall, from which thromboplastic substances might be liberated, were factors in the precipitation of venous thrombi. It is well recognized, of course, that inflammatory foci may initiate thrombophlebitis, but foci of this type have never been demonstrated in the type of thrombosis under discussion—phlebothrombosis. The elucidation of the problem has been

hampered by the fact that venous thrombi are usually so inordinately long that it is hard to demonstrate conclusively the presence or absence of an injury to the vein wall at the point of primary thrombus deposition. Arterial thrombi do not present this difficulty. Coronary thrombi, for example, rarely measure more than an inch in length, and the primary injury (an intimal hematoma) can be easily demonstrated by serial section technique (12). But to attempt a complete serial section of a thrombosed segment of vein, which may measure many inches in length, is a formidable undertaking; and if anything less than a complete serial section is done, a small precipitating lesion in the vein wall may easily be missed. We have overcome this difficulty by restricting our studies to tiny, incipient thrombi—thrombi so small that they can easily be handled by the complete serial section method. In the course of our 165 dissections, we have succeeded in obtaining 21 incipient thrombi of this type for special study.

Each of the thrombosed segments of vein was similar in size to that illustrated in Figure 1. It was removed *in toto*, fixed in formalin, and embedded in paraffin in one piece. Sections of 6 microns thickness were cut in ribbons through the entire length of the thrombus, the ribbons being stretched flat on cardboard. Every thirtieth section was then mounted, stained with hematoxylin and eosin, and examined microscopically. These preliminary sections indicated the approximate earliest site of thrombus deposition (as manifested by the degree of organization of the thrombus), and thereafter every section in the vicinity of this primary deposit was mounted, stained, and examined.

Additional blocks of vein wall were taken at random from representative sites in each of the first 100 cases on which venous dissection was practiced. They were taken routinely from the common femoral vein, the long saphenous vein, the profunda femoris vein, the popliteal vein, the posterior tibial vein, and from the point of maximal phlebosclerosis as determined by gross examination. Single sections of these blocks were stained with hematoxylin and eosin and were studied for

Fig. 1. Photograph of the dissected specimen from a case of incipient venous thrombosis. The arrow points to a small thrombus, measuring about 1 centimeter in length, lying in the profunda femoris vein. Thrombi of this size were chosen for complete serial section.

those lesions which might conceivably be related to thrombosis. They included inflammatory infiltration of the vein wall, the degree of phlebosclerosis, vascularization and hemorrhage of the intimal layer, and atheromatous degeneration or calcification. When lesions were present, an attempt was made to relate them to the tendency to thrombosis.

The results of these morphologic studies have been so conclusive that we feel justified in stating, categorically, that local injury or disease of the vein wall, of an obvious type, plays no part in the precipitation of bland thrombi in the veins of the lower extremities.

Microscopic examination of the random sections from various parts of the veins showed the degree of generalized phlebosclerosis to be no greater in the cases with thrombosis than in those without thrombosis. And when thrombi were present, they were just as apt to occur at points of lesser degrees of sclerosis as at points of severe disease. Vascularization of sclerotic plaques was often a prominent feature, and occasionally it had resulted in intimal hemorrhage. However, no instance of thrombus deposition at a point of intimal hemorrhage was seen. Calcification of the vein wall did not appear to play any part in the tendency toward thrombosis. Inflammatory infiltration of some part of the vein wall was observed in 30 per cent of the cases with thrombi and in approximately 12 per cent of those without thrombi. The infiltration consisted of a slight

spattering with lymphocytes, and it had no apparent relationship to the site of thrombus precipitation except in cases of frank thrombophlebitis.

The most impressive negative evidence on the role of local injury was obtained from complete serial section of the 21 incipient venous thrombi in our series. These thrombi were traced to their points of primary deposition, and there they failed, in every case, to show any lesion in the vein wall that might have acted as the precipitating mechanism. A slight degree of lymphocytic infiltration was seen in the vein wall in 4 of the 21 cases, but it was not impressive either in its severity or in its frequency. When it did occur, we were inclined to attribute it to the thrombus, which had interfered with the nutrition of the vein wall by blocking the normal process of imbibition, rather than to infection.

THE FACTOR OF ABNORMAL BLOOD COAGULABILITY

Many substances, when present in abnormal quantities in the blood, have been suggested as the cause of bland venous thrombosis. We have evaluated their importance by comparing their antemortem levels in seriously ill patients with the pathologic findings in those patients who died and came to autopsy. The method is simple, although arduous. As soon as a patient's name appeared on the critically ill list of our hospital, his blood was examined for the appropriate material twice a week, and this was repeated until he either died or recovered. If he died and came to autopsy, venous dissection of the lower extremities was practiced, and the presence or absence of venous thrombi was noted and confirmed by microscopic examination. The antemortem biochemical findings in the 6 weeks' period before death and the postmortem findings were then compared. This technique has been used in the last 69 cases in our series, and from these cases we have evaluated the importance of the total fibrinogen, fibrinogen B, antithrombin, fibrinolysin, alpha tocopherol, and the platelet count of the blood. Detailed reports for each of these evaluations will be published elsewhere, and only the major findings will be given here.

Blood antithrombin. Our evaluation of the antithrombin test has already been published (9). In summary, we have assessed the claims of Kay and Ochsner that a reduction of the blood antithrombin level, as revealed by their test, indicates a prethrombotic tendency that calls for immediate therapy. Our experience has been that dangerously low antithrombin levels are rarely present in those patients who subsequently die and show definite venous thrombi at autopsy. And from this we have concluded that the antithrombin test of Kay and Ochsner is of no value in predicting incipient venous thrombosis under ordinary hospital conditions.

Blood fibrinogen B. The fibrinogen B level, which has also been claimed to reflect a prethrombotic tendency, has yielded negative results in our hands. Serial determinations of this material were carried out on the blood of a large series of critically ill patients, using the exact technique stipulated by Cummine and Lyons. Twenty-five of these patients died, and at autopsy venous thrombi were present in 11 and absent in 14. Only 3 of the 11 patients with proved thrombi (27 per cent) had shown a fibrinogen B level in the so-called dangerous range during life, while 2 of the 14 patients without venous thrombosis had shown similar "dangerous" blood levels of the material (14 per cent). It is thus apparent that false positives are not infrequent with this test, and that true positives are obtained so rarely that the test is of little practical value.

Blood fibrinogen. Excess of blood fibrinogen has been said to accelerate the sedimentation of blood in vitro. Best and Taylor state that fibrinogen increase is seen in a number of pathologic conditions including thrombosis. Brinkhous claims that patients who develop thrombosis have high plasma levels of fibrinogen and globulin. Serial determinations of this material, using a gravimetric technique, have been carried out, twice a week, on a large number of critically ill patients, of whom 62 died and were subjected to venous dissection at autopsy. Between 4 and 5 fibrinogen determinations had been done on each of these patients in the 6 weeks' period before death. In 29 cases without venous thrombosis, the

average blood fibrinogen level was 545 milligrams per cent (SEM ± 34), while in the 40 cases with thrombi the average level was 469 milligrams per cent (SEM ± 29). Analyzed statistically, using a comparison of the standard error of the means, the difference between the two groups is not significant (P = >0.1). It can also be seen that the average blood level of fibrinogen was lower in the thrombotic group than in the non-thrombotic group—a result that is distinctly against the theory.

Blood alpha tocopherol. Kay and Ochsner have claimed that alpha tocopherol is a potent antithrombin; that if it is present in the blood in adequate quantities the tendency to venous thrombosis should be inhibited. We have already shown that the antithrombin test of Kay and Ochsner is of no value in predicting incipient venous thrombosis under ordinary hospital conditions (9), but in the present study the blood level of alpha tocopherol was compared directly with the presence or absence of thrombi. Blood determinations were done serially on a large number of critically ill patients, of whom 24 died and were subjected to venous dissection at autopsy. The antemortem determinations of alpha tocopherol were done by the modified method of Quaife, Scrimshaw, and Lowry. An average of 5 determinations was made on each patient in the 6 weeks' period before death. In 10 cases without venous thrombosis, the average blood level of the material was 0.91 milligram per cent (SEM ± 0.07), while in the 14 cases with thrombosis it was 0.79 milligram per cent (SEM ± 0.06). These results were analyzed statistically by a comparison of the standard error of the means, and the difference between the two groups is not significant (P = >0.2). Thus, whether or not alpha tocopherol has antithrombin properties, it had no obvious effect in altering the tendency to venous thrombosis in our series.

Blood fibrinolysin. By a process of rather devious reasoning, it might be assumed that the primary deposition of small thrombi in veins might be aborted by the presence in the blood of fibrinolytic substances. This mechanism has been suggested by Mole for the dissolution of small mural thrombi in arteries,

Fig. 2. Low power photomicrograph of part of a complete serial section through an incipient venous thrombus. The direction of blood flow was from below upward. The thrombus completely fills a valve pocket. At its apex (marked with the arrow) it showed extensive organization, while proximally, it was progressively younger in age. Heidenhain, × 10.

and if true it should be applicable equally to veins. We have investigated this possibility by carrying out determinations of blood fibrinolysins, twice a week, on critically ill patients, and have compared the results with the presence or absence of venous thrombi in 69 patients who died and were autopsied. The determinations were done after the method of Macfarlane, and an average of from 4 to 5 tests was done on each patient in the 6 weeks' period prior to death. In 29 cases without thrombosis in our series, 10 individuals showed a loss in fibrin of more than 0.3 milligram (the margin of error by our technique is less than this figure). In 40 cases with thrombi, 19 cases showed a fibrin loss greater than this amount. Analyzed statistically by the chi-square test, the difference between the two groups is not significant (P = >0.3). We are, therefore, not impressed with the effect of fibrinolysis on the resolution of thrombi in veins once they are formed, although it may

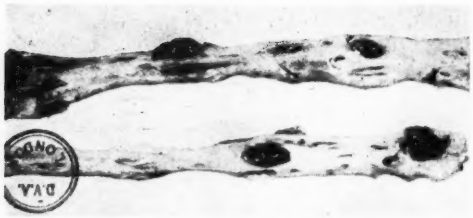

Fig. 3. The right and left superficial femoral veins from a case of incipient venous thrombi. Four distinct thrombotic masses are lying in valve pockets. It is to be noted that only one of each pair of valves is involved, and that the same valve of each pair contains the thrombus, suggesting a possible effect from posture. The direction of blood is from left to right.

play some part in the fragility of formed thrombi and in the production of pulmonary embolism. We intend to discuss this latter point in some detail elsewhere.

Blood platelets. Finally, it has been suggested by Gage that abnormalities in the quality or quantity of blood platelets may be concerned in the mechanism of venous thrombosis. We have counted the number of blood platelets, after the method of Moolton and Vroman, in a series of critically ill patients, of whom only 6 have died and been autopsied to date. From 3 to 4 determinations were done in each case in the 6 weeks' period before death. In 2 cases without venous thrombi, the average platelet count was 293,000 per cubic millimeter of blood, while in 4 cases with thrombi the average count was 332,000. The series is too small for a definite conclusion to be drawn, but it would seem that the platelet count is of little value in predicting incipient venous thrombosis.

THE FACTOR OF VENOUS STAGNATION

Stasis of blood in veins, and in other circulatory channels, has long been suspected as a major precipitating factor of thrombosis. Suspicion has even reached the stage of conviction among certain investigators, and prophylactic measures have been elaborated to combat venous stasis in the lower extremities and thus prevent thrombosis, as indicated by Wilkins and co-workers. Our studies have convinced us that these suspicions are justified.

If thrombi are examined in their early stages, before they completely occlude the lumen of the vein, they can be seen to originate in those locations where stagnation of blood should be maximal—in the cul-de-sacs formed by valve pockets. Our findings in this regard were clear cut. As mentioned previously, we have had the opportunity of examining by serial section 21 tiny incipient thrombi of a size like the one illustrated in Figure 1. Seventeen of these, or approximately 80 per cent, have been found to originate in valve pockets. The usual site for thrombus attachment was at, or near, the apex of the pocket—at the point where stasis of blood should be most extreme. Microscopically, the thrombi showed the greatest degree of organization at these points, and they had a more recent structure as they extended up the pocket before emerging from its mouth. Microscopic appearance of one of these small thrombi is shown in Figure 2.

Gross examination of all thrombi in our series, large ones as well as small ones, confirms this observation on the importance of the valve pockets, although the findings were not nearly so impressive. In the course of our first hundred venous dissections we encountered 76 individual thrombotic masses. Some of these were small while others were extremely long, extending from the ankle to the pelvis. Twenty-three of these masses, or 30 per cent, appeared to originate in valve pockets. Some of these thrombi, especially when they were small and multiple, presented a striking gross picture, and these are shown in Figures 3, 4, and 5.

DISCUSSION

From the foregoing, it is apparent that neither local injury to the vein wall, of an obvious type, nor abnormality in those blood coagulation factors that were studied, was concerned in the precipitation of the venous thrombi in our series. We are, therefore, inclined to minimize the importance of these two factors in the mechanism of bland venous thrombosis in general, although it is conceded that they may operate in exceptional cases.

By elimination, then, the factor of venous stasis achieves some importance in our thinking; and this is further strengthened by the deductions arising from our indirect observations. To incriminate venous stagnation def-

Fig. 4. Photograph of an opened superficial femoral vein showing two small thrombi arising from the valve pockets at one point.

Fig. 5. Large thrombus, arising from a single valve pocket in the superficial femoral vein and showing grossly visible lines of Zahn. It had resulted in a pulmonary embolus.

itely as the cause of phlebothrombosis it ould be necessary to make serial determinaons of blood flow in the veins of the legs uring life and then to correlate these deterninations exactly with the presence or abence of venous thrombi at autopsy. We have ot attempted this crucial experiment, but ave relied on the indirect evidence described n this report. When venous thrombi were letected in their early stages they were found o arise, almost invariably, in valve pockets, a location that is assumed to be most susceptible to stagnation of blood. Larger and older thrombi do not show this peculiar localization; but this discrepancy can be easily explained. After originating in a valve pocket, a thrombus will propagate proximally until it eventually occludes the lumen of the vein. A column of stagnant blood will be produced by the occluding mass, and this should lead to propagation in the opposite direction. The thrombus will now overflow the valve pocket and extend distally, thus obscuring the site of primary deposition. If this be true, it explains why the origin of venous thrombi in valve pockets has not been stressed by previous workers in the field. They must obviously have studied end-stage lesions, not early ones.

One can only speculate on the possible changes that occur at the apices of valve pockets and result in the initial thrombotic mass. Like other vascular channels, a vein depends on the imbibition of substances from the blood in its lumen for the nutrition of its inner layers. With venous stagnation, these substances, including oxygen, will be depleted; and it seems reasonable to suggest that morphologic changes of a highly intimate type occur in the lining endothelial cells and lead to the primary thrombus deposition. We have tried to demonstrate such changes; but our efforts have been unsuccessful, perhaps because of the inadequacy of our methods. Newer techniques, like those utilized by Samuels and associates, in which the endothelial layer of blood vessels is made accessible to direct study, may throw light on the exact mechanism of thrombosis in the valve pockets of veins.

In conclusion, it is our firm conviction that the prophylaxis of phlebothrombosis in the lower extremities hinges on the preservation of an efficient venous return from these parts. There is no originality in this conclusion, but the observations recorded in this paper should strengthen the suspicions of those who already

adhere to the same view. We intend, in the near future, to discuss the efficacy of the many measures that have been suggested in the past for preventing venous stagnation in postoperative cases; and for the present would merely remind readers of this paper that posture is an important factor. Using modern tracer methods, Wright and Osborn have shown that elevation of the lower extremities by as little as 10 degrees above the horizontal doubles the venous flow rate in the legs.

SUMMARY AND CONCLUSIONS

Current theories on the etiology of phlebothrombosis have been evaluated from a study of 165 fatalities on which venous dissection of the lower extremities was practiced at autopsy. The theories evaluated have been those concerned with local injury to the vein wall, with abnormal blood coagulability, and with venous stagnation.

Complete serial section of 21 incipient venous thrombi has shown, conclusively, that local injury or disease in the vein wall (of an obvious type) is not a factor in the precipitation of bland venous thrombi in the lower extremities.

Comparisons of antemortem blood levels of fibrinogen, fibrinogen B, antithrombin, alpha tocopherol, fibrinolysin, and of the blood platelet count with the presence or absence of venous thrombi in patients who subsequently died, have failed to show any etiologic relationships in our series. It is concluded that abnormalities in blood coagulation, of the types studied, are not important factors in the etiology of the disease.

The striking tendency of venous thrombi, especially incipient thrombi, to be initiated at the apices of valve pockets suggests that venous stagnation is a major factor in the etiology of phlebothrombosis. Measures aimed at improving the venous return from the legs in postoperative cases are, therefore, recommended for the prevention of thromboembolic disease.

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ANATOMIC VARIATIONS AND PATHOLOGIC CHANGES IN COARCTATION OF THE AORTA

A Study of 124 Cases

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COARCTATION of the aorta is a congenital narrowing or stricture usually occurring just distal to the origin of the left subclavian artery. With the development of surgical treatment of coarctation of the aorta by such workers as Crafoord and Nylin and Gross and Hufnagel, the anatomic variations of this lesion, which had previously been of academic interest only, became a matter of great practical importance. Although much has been written about various aspects of coarctation of the aorta in recent years, such reports have not emphasized these anatomic variations and pathologic changes that may occur in the aorta and its branches at and near the site of stricture. To elucidate these variations, we have reviewed the records in 124 cases of coarctation of the aorta in which surgical exploration has been done at the Mayo Clinic.

CLASSIFICATION OF COARCTATION

The terms "infantile" and "adult" types of coarctation of the aorta have not been found of great use in classification. From both clinical and surgical viewpoints, desirable classification should take into account the following two major considerations: (1) the relative position of the coarctation and the ductus arteriosus and (2) the patency of the ductus arteriosus. Such a classification is that of Johnson and associates.

The following classification, which uses the principles just mentioned, is useful (Fig. 1): (A) coarctation distal to the ductus arteriosus—(1) ductus arteriosus closed and (2) ductus arteriosus patent; (B) coarctation proximal to the ductus arteriosus—(1) ductus arteriosus closed and (2) ductus arteriosus patent.

In addition to the factors indicated in this classification, the clinical picture encountered and the surgical techniques employed may be modified as a result of special or additional features. Hypertension in the right arm, as measured by the cuff method, accompanied by feeble pulses in the left arm (Fig. 2) may result from: (1) atresia of the left subclavian artery; (2) stenosis of the left subclavian artery; or (3) coarctation proximal to the left subclavian artery. Clinically evident hypertension in the left arm and feeble pulses in the right upper extremity (Fig. 2) may result from: (1) stenosis of the right subclavian artery or (2) origin of the right subclavian artery as the fourth branch of the aorta at a point beyond the coarctation.

SEX AND AGE OF PATIENTS

In this series of 124 patients who had coarctation of the aorta, 42 were females and 82 males. It is stated usually that this lesion occurs four or five times as frequently in males as in females. However, most reported series of cases of coarctation of the aorta have been collected from material obtained at necropsy, while this series consists of patients well enough to have been subjected to surgical exploration; thus selection of patients in this series may be responsible for the difference in sex incidence. It has been our experience, as will be detailed subsequently, that serious cardiovascular damage and complications are more likely to develop in males than in females; therefore, some male patients who had coarctation may have been denied surgical exploration because of their poor condition. In any event, coarctation does occur more

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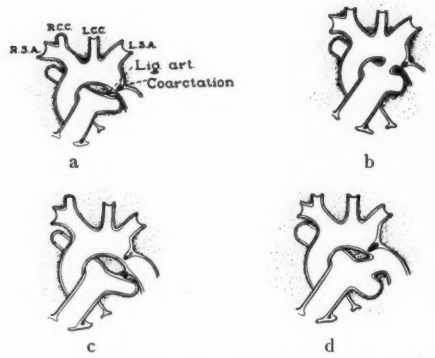


Fig. 1. Classification of coarctation. a and b, Coarctation distal to ductus arteriosus; a, ductus arteriosus closed and b, ductus arteriosus patent. c and d, Coarctation proximal to ductus arteriosus; c, ductus arteriosus closed and d, ductus arteriosus patent.

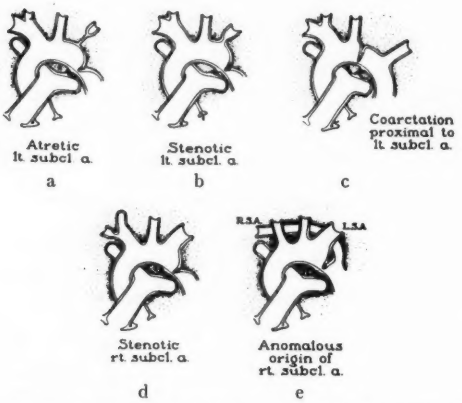


Fig. 2. Anatomic variations responsible for unequal blood pressures in the two arms. In a, b, and c, elevation of blood pressure is present in the right arm, with feeble pulses in the left. In d and e, the pulses in the right arm are feeble and elevation of blood pressure is present in the left arm.

commonly in males and it is not possible to explain this difference. This fact is of particular interest, since patent ductus arteriosus, another relatively common congenital cardiovascular anomaly occurring in an adjacent anatomic area, is present more commonly in females.

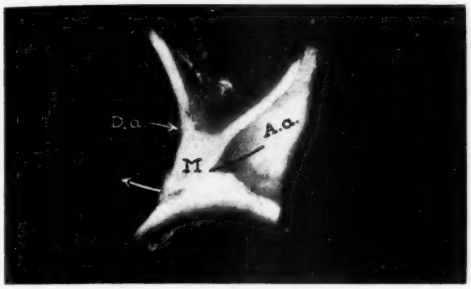
The ages of this series of patients at the time of operation varied greatly: 3 patients were in the first decade of life; 17 were between 10 and 14 years old; 19 between 15 and 19 years; 35 between 20 and 24 years; 24 between 25 and 29 years; 16 between 30 and 34 years; 6 between 35 and 39 years; 3 between 40 and 49 years; and 1 was over 50 years of age. The youngest patient on whom operation was performed was 10 weeks of age, and the oldest patient was 50 years of age. It is not difficult to explain why most of the patients in this series were from 20 to 30 years of age at the time of operation. The presence of coarctation usually is not discovered in infants and children but most commonly is suspected first when young adults who are being examined for school, insurance, the armed services, or employment are found to have elevated blood pressures, as determined by means of the arm-cuff method. The infrequency of patients more than 30 years of age in this series is due to the fact that many patients who have coarctation have incurred complications or such serious cardiovascular damage that surgical exploration is not advisable, while others have died of one of the complications. According to Reifenstein and associates, 74 per cent of patients who have coarctation of the aorta die as a result of the lesion before the age of 35. However, about a fifth of the patients in this series were more than 30 years of age. We have not considered that chronologic age in itself contraindicates operation.

NATURE OF COARCTATION AND LENGTH OF STRICTURE

The most striking change in coarctation involves an extremely short segment of the aorta. In some cases this may be the only part of the aorta that displays narrowing, while in other cases the aorta in the vicinity of this most striking change may be considerably narrowed.

In this study the term "length of stricture" refers to the zone of greatest narrowing in addition to any significant narrowing in the region of the basic lesion.

As has been described by one of us (Edwards) and associates, the aortic wall at the site of the most striking change shows a curtainlike infolding of the media that involves the superior, anterior, and posterior aspects



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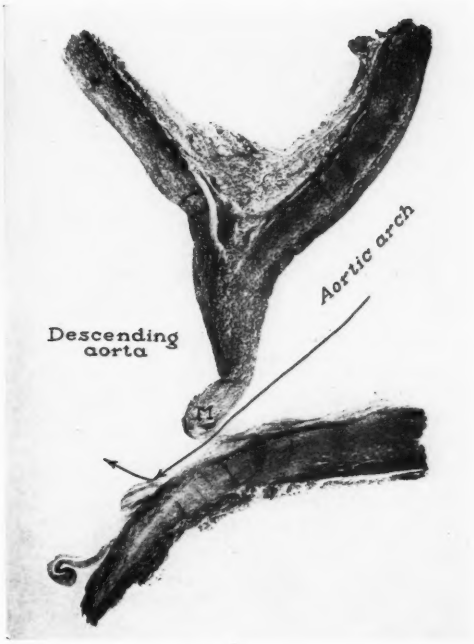


b

Fig. 3. Segment of aorta with coarctation removed surgically from a 30 year old woman; specimen viewed from behind. a, A longitudinal section has been made in the gross specimen and the posterior wall of the aorta has been removed. The infolding of the media of the upper wall (*M*) caused considerable luminal narrowing. *A.a.*, aortic arch; *D.a.*, descending aorta. b, Same specimen. Profound luminal narrowing has resulted from infolding of the media (*M*) of the superior portion of the aortic wall. The external diameter of the vessel is considerably wider than the lumen at the point of coarctation. Mild intimal thickening is present in the lower wall just proximal and distal to the coarctation (ELVG[1], ×3.7).

of the aorta (Fig. 3). The lower portion of the aortic wall, or that portion into which the ductus arteriosus inserts, does not take part in the deformity. This part of the wall may be unaltered but, if it is deformed, it everts toward the ductus instead of protruding toward the lumen, as the rest of the aorta does at this level. The external diameter of the aorta, although narrow, is considerably wider than the diameter of the lumen (Fig. 4).

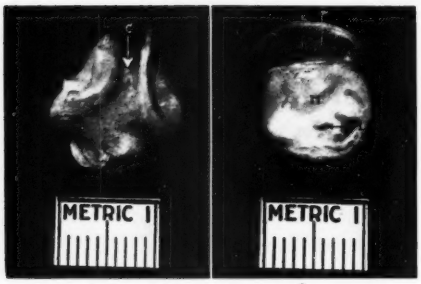
Although earlier workers have suggested that the aortic coarctation is related to overgrowth of tissue of the ductus arteriosus into the aortic wall, we have not been able to substantiate this claim after histologic examination in a large number of cases, in some of which reconstructions of serial sections were prepared and studied.

No positive opinion can be given in regard to the developmental basis for the curtainlike infolding of the aortic media. It will be recalled, however, that the part of the aorta involved in the anomaly is that part in which profound changes normally occur during early stages of development. In such early stages of aortic development, the subclavian arteries arise caudad to the sixth aortic arches, from the left one of which the ductus arteriosus is derived. As development progresses, the left subclavian artery comes to lie cephalad to the ductus arteriosus. Such a profound alteration, in which the relative position of vessels changes, must involve considerable degrees of differential growth. It is perhaps during such processes that abnormal degrees of differential growth produce a relatively excessive amount of aortic tissue; this redundant tissue then protrudes like a curtain into the aortic lumen.

Indirect support of such a concept comes from our observation that when the coarctation was proximal to the left subclavian artery, the latter vessel had not reached its normal definitive position but was distal to the ductus arteriosus (Fig. 5).

It is interesting to consider the interpretation of the histologic appearance of the coarc-

[1]The abbreviation ELVG used here and subsequently designates Verhoeff's elastic-tissue stain counterstained with van Gieson's connective-tissue stain.



a b

Fig. 4.

Fig. 4. a, Anterior view of segment of aorta with coarctation removed surgically from a 34 year old man. The external diameter of the aorta, although narrow, gives little indication as to the position and caliber of the actual lumen. *L.A.*, ligamentum arteriosum; *C*, area of coarctation. b, Same specimen viewed from below. Note the diaphragmlike deformity of the aortic wall (*M.*) causing pronounced luminal narrowing and eccentric position of the lumen (*L.*), which is nearer the lower wall than the upper.

Fig. 5. Segments of aorta, ductus arteriosus and left subclavian artery removed surgically from a 4 year old boy. a, Specimen viewed from front. A probe passes from the proximal portion of the aorta through the aortic mouth of the patent ductus arteriosus; another probe passes from the descending aorta through the aortic mouth of the patent ductus arteriosus. The coarctation (*C.*) is proximal to the left subclavian artery (*L.S.*). b, Same specimen viewed from above. Note the diaphragmlike infolding of the aortic wall (*M.*), creating a narrow eccentric aortic lumen (*L.*) beneath it. The stump of the divided left subclavian artery (*L.S.*) is shown also. c, Same specimen viewed from below. Note the mouth of the left subclavian artery (*L.S.*) distal to the coarctation (*M.*). A portion of the aortic mouth of the patent ductus arteriosus (*P.D.A.*) is shown. d, Same specimen viewed from behind. The coarctation is opposite the aortic mouth of the patent ductus arteriosus and proximal to the origin of the left subclavian artery (*L.S.*). A peculiarity of coarctation proximal to the left subclavian artery is illustrated in this case, in which the origin of the left subclavian artery is distal to the aortic mouth of the ductus arteriosus (ELVG, ×5.4).

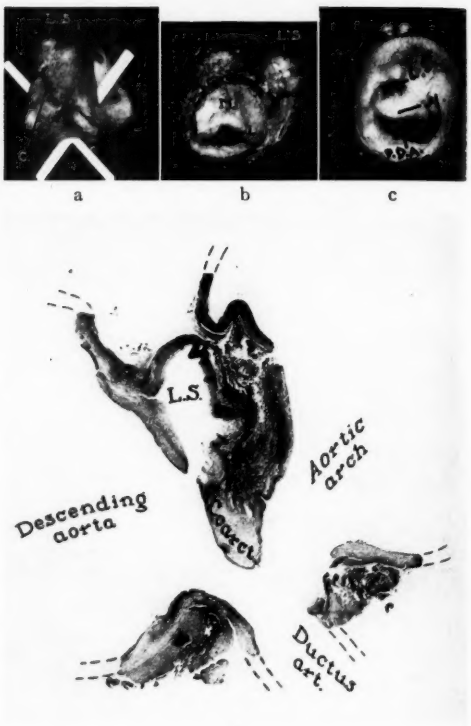


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Fig. 5.

tation in terms of the gross aortic structure at the involved segment (Fig. 6). The infolding of the media produces a diaphragmlike membrane across most of the aortic lumen, which is thus narrowed. The small opening is placed eccentrically near the lower aortic wall. The hourglass deformity of the aorta with a central perforation that is so frequently described and drawn must be viewed as an inaccuracy. The diaphragm across the aortic lumen is basically made up of the deformed media but, in older patients, secondary intimal fibrous thickening is present not only in the aorta proximal to the coarctation but also at the edges of the narrow aortic lumen.

Because the force of the blood is directed distally, the diaphragm tends to bulge distally, somewhat in a funnel fashion; fibrous overgrowth at the edges of the narrow opening may bulge nipplelike into the distal segment (Fig. 7). It is common for ridges of intimal fibrous thickening to extend along the intima of the distal segment from the narrowed lumen. Such ridges appear to represent secondary effects of the trauma caused by the blood that flows through the aortic lumen.

In most cases in this study, an aortic lumen was present but rarely did it measure more than 2 millimeters in diameter. In some cases, the lumen was closed completely. At times the closure appeared to result from organization of a thrombus in the narrowed lumen.

Great variation in the length of the aortic stricture was noted in these 124 cases of coarc-

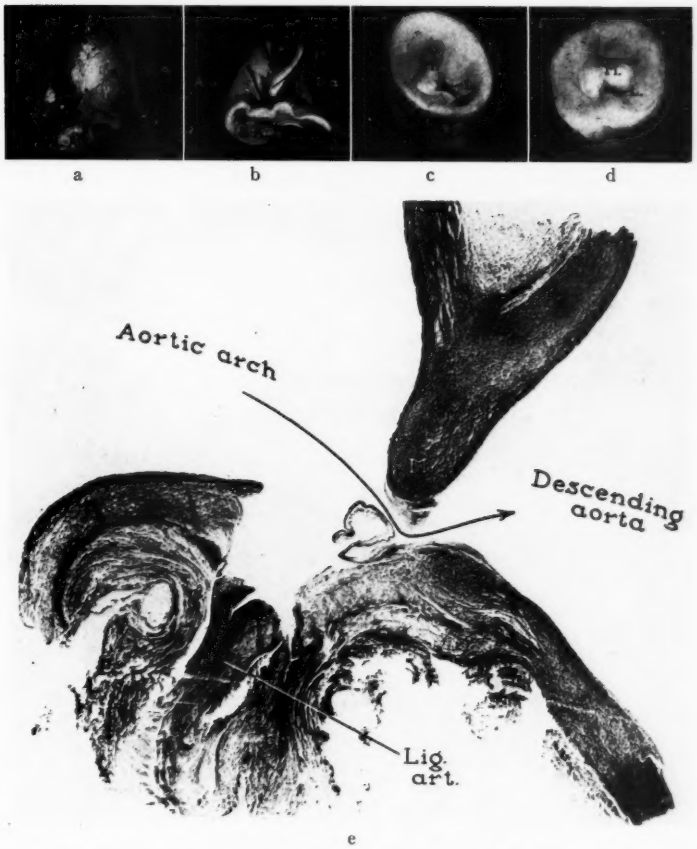
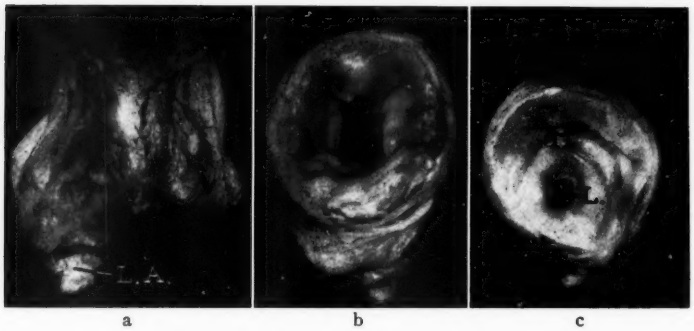


Fig. 6. Segment of aorta with coarctation removed surgically from a 20 year old man. a, Specimen viewed from front. The upper wall shows a mild concave deformity (arrow) at which point the interior of the aorta, shown in other illustrations, is represented by a greatly narrowed lumen. *A.a.*, aortic arch; *D.a.*, descending aorta; *L.A.*, ligamentum arteriosum. b, Longitudinal section of specimen viewed from front showing infolding of media (*M.*) causing eccentricity and profound luminal narrowing. c, The coarctation viewed from above showing the eccentric and narrow lumen (*L.*) and the mild funnellike deformity of the diaphragm (*M.*). d, The coarctation viewed from below showing the downward deflection of the diaphragm (*M.*) and the eccentric and narrow lumen (*L.*), which is near the lower wall. e, Specimen viewed in same perspective as in b. The extensive curtainlike deformity of the aortic media (*M.*) produced profound luminal narrowing at a point just distal to the junction of the ligamentum arteriosum (*Lig. art.*) with the lower wall of the aorta. Minimal intimal thickening is present at the apex of the curtainlike deformity of the media. An artefact is present at the insertion of the ligamentum arteriosum (ELVG, ×5.6).

tation of the aorta. In some the stricture was relatively long and tapering, whereas in others it was extremely short with a practically normal-sized aorta both above and below the stricture itself. It was not possible to anticipate the size of the lumen at the site of the stricture by examination of the exterior of the aorta. In a few cases, only slight narrowing of the aorta was apparent from external examination, yet the lumen was almost occluded by a diaphragm (Fig. 4). In 83 cases, according to the surgeon's estimate, the length of the



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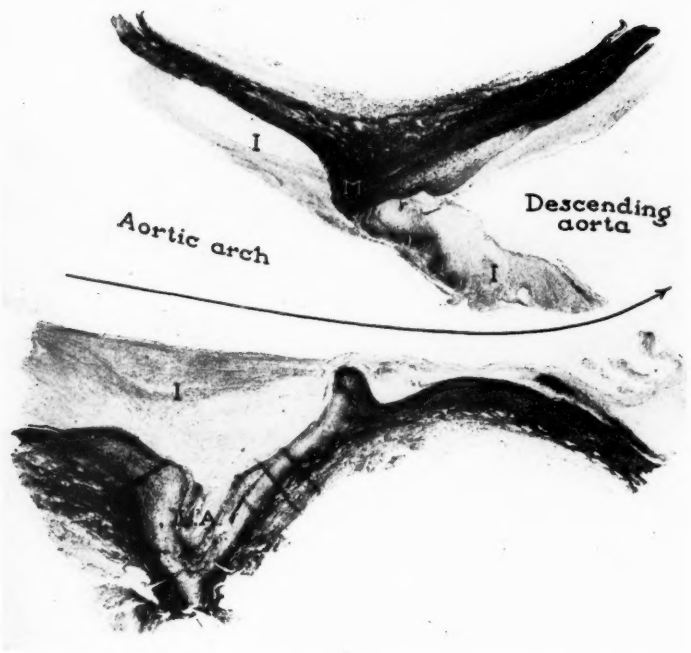

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Fig. 7. Segment of aorta with coarctation removed surgically from a 36 year old man. a, Specimen viewed from front. Note the ligamentum arteriosum (*L.A.*) at the proximal portion. b, Coarctation viewed from above. Note the funnellike deformity directed downward. The wall is thickened by the presence of considerable amounts of intimal fibrous tissue. c, Coarctation viewed from below. The diaphragmlike deformity (*M.*) and the narrow lumen (*L.*) lying eccentrically near the lower wall are shown. d, Specimen oriented as in a. In addition to the deformity of the media (*M.*) representing coarctation at a point distal to the aortic end of the ligamentum arteriosum (*L.A.*), great intimal thickening (*I*) is present in the aorta proximal to and at the point of the coarctation. In the latter position, this intimal fibrous tissue contributes to the diaphragm and tends to narrow the lumen somewhat beyond the degree created by the basic deformity of the media. The distal protrusion of the intimal component of the diaphragm is striking and accounts for the nipplelike protrusion seen about the lumen in c (ELVG, ×4.6).

resected specimen was about 1.5 centimeters. In 20 cases, approximately 2 centimeters of the aortic length was removed. In 1 case, centimeters of aorta were resected, whereas in 1 other case, only 1 centimeter was removed. In 11 cases, the condition was considered inoperable for a variety of reasons and the stricture was not removed. For a number of technical reasons, the stricture was not resected in 8 cases encountered early in our experience. Instead, the site of stricture was ligated and the aorta was transected distal to the stricture; the left subclavian artery was divided, the distal end ligated and the proximal end rotated over and anastomosed to the distal aortic segment. Because of technical difficulties in 1 case in which the stricture of the aorta was resected, it was necessary to suture the proximal portion of the aorta and then rotate the subclavian artery over for anastomosis to the aorta.

RELATION OF COARCTATION TO THE LEFT SUBCLAVIAN ARTERY

While coarctation of the aorta usually occurs at a point just distal to the origin of the left subclavian artery, considerable variation in its location may occur: in 4 cases of our series it was found proximal to the left subclavian artery; in 2 involving it; 5 millimeters distal to the artery in 24 cases; 1 centimeter distal to it in 30 cases; 1.5 centimeters distal to it in 38 cases; more than 1.5 centimeters distal in 25 cases; and in 1 instance the site of stricture (aneurysm) was not determined. This variation is of considerable importance to the surgeon, since this factor determines to a large degree how easy or how difficult the operation may be.

In 4 cases, the stricture of the aorta was located proximal to the origin of the left subclavian artery (Fig. 5) and in these cases, of course, elevation of blood pressure as determined by the cuff method was limited to the right arm; evidence of collateral circulation, as determined by means of thoracic roentgenograms and physical examinations, also was limited to the right side. In 2 cases, the stricture occurred exactly at the origin of the left subclavian artery, which was an obliterated fibrous cord. In most cases, the coarctation

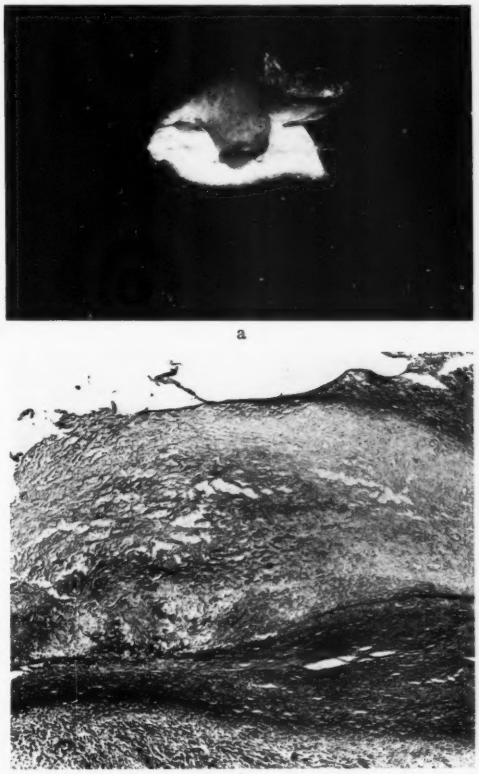

Fig. 8. Segment of aorta with coarctation removed surgically from a 20 year old woman; specimen viewed from front. a, Specimen has been sectioned longitudinally and the anterior wall has been removed. A probe is in the aortic lumen at the coarctation. A large atheromatous plaque is proximal to the probe and at the site of connection of the ligamentum arteriosum with the lower aortic wall. b, Atheromatous plaque shown in a (ELVG, ×7).

was situated 0.5 to 2 centimeters distal to the origin of the left subclavian artery. In only 1 case in this series was the stricture located more than 3 centimeters from the origin of the left subclavian artery. However, cases of coarctation have been reported in which the stricture has occurred in more distal portions of the thoracic aorta. In 1 of our cases, an aneurysm about 4 centimeters in diameter was discovered near the site of stricture. Resection of the aneurysm with anastomosis of the aorta was not possible and the exact relationship of aneurysm to stricture was not determined.

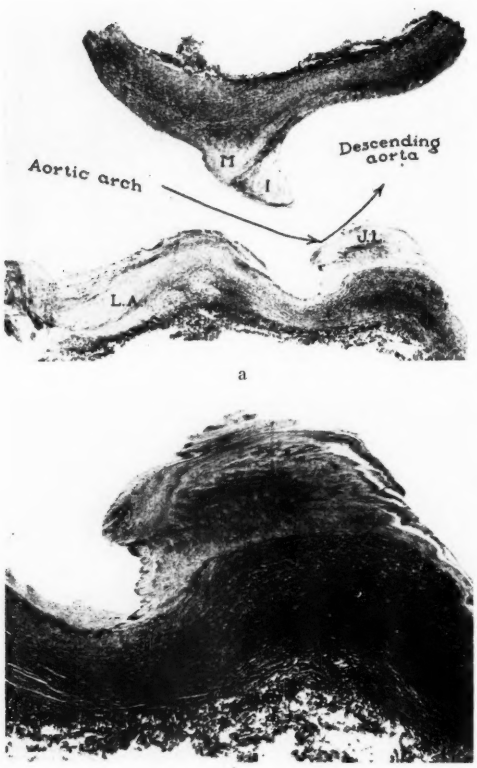

Fig. 9. Longitudinal section of segment of aorta removed surgically from a 19 year old man; specimen viewed from front. a, The medial deformity (*M*) of the superior wall produces a curtainlike infolding of the media. Superimposed on the medial curtain is proliferated intimal fibrous tissue (*I*). In the distal segment of the aorta and at the position presumably traumatized by the stream of blood passing through the narrowed aortic lumen, is a focal zone of fibrous thickening (*J.L.*) representing a jet lesion (ELVG, ×3.8). b, Jet lesion illustrated in a (ELVG, ×17).

CHANGES IN THE AORTIC WALL

Except at the site of coarctation, where profound structural alteration is present in the aortic media, the media both above and below the stricture is usually normal histologically. The relative amount of media, however, may be somewhat less than normal below the coarctation. The intima exhibits greater evidence of alteration than does the media and appears to reflect the peculiar stresses imparted by the narrowing of the aortic lumen.

Proximal to the coarctation, these intimal alterations, if present, are manifested by a general increase in fibrous tissue, usually densely collagenous in nature, with deposits of variable amounts of elastic fibers within this new tissue (Fig. 7). Less common and less general than this type of nonspecific intimal thickening are intimal atheromatous plaques with or without calcification (Fig. 8).

Regardless of the nature of the intimal thickening in the proximal segment, the altered intima is indurated, relatively inflexible, and is poorly attached to the underlying media. The latter features of the altered intima particularly are technical hazards, since these changes interfere with eversion of the vessel for proper suturing during surgical manipulation; also the thickened intima may become separated from the media, interfering potentially with a durable anastomosis.

While the changes in the proximal segment frequently are general and presumably are the effects of general stresses in that component of the aorta, intimal changes in the distal segment are focal and probably are the result of localized traumatic effects of the jetlike stream of blood flowing through the narrow aortic lumen (Fig. 9). The location of these changes, which usually are characterized by nonatheromatous intimal thickening, depends on peculiarities in angulation of the aorta and on the orientation of the lumen at the zone of coarctation. If the jetlike stream strikes the aortic wall directly, an intimal lesion, the so-called jet lesion, is apt to develop at that particular region. Should the jet be directed into the central part of the distal aortic lumen, no secondary lesion develops.

The significance of localized lesions in the distal portion of the aorta is manifest. Should a lesion be within the field of resection, the thickened intima may present problems concerned with proper anastomosis. The localized lesions of the intima may be followed by weakness of the underlying media and formation of aneurysms or the intimal lesion may represent a site for bacterial infection, which in turn may become complicated by the presence of a mycotic aneurysm.

It is well known that if the hypertension and altered hemodynamics produced by coarcta-

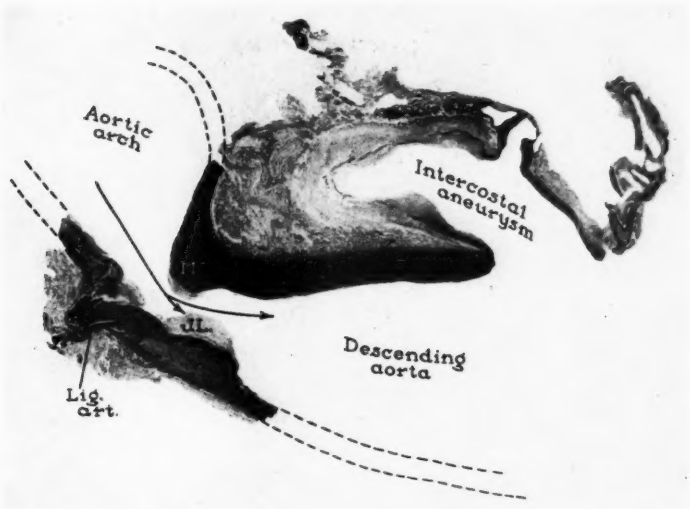

Fig. 10. Segment of aorta and aneurysm of intercostal artery removed surgically from a 24 year old woman; specimen viewed from front. The medial deformity (*M*), representing the coarctation, is just distal to the ligamentum arteriosum (*Lig. art.*). A small jet lesion (*J.L.*) is present in the distal segment. The aneurysm, which is continuous with the upper aortic wall, represents an aneurysm of an intercostal artery (ELVG, ×3).

tion of the aorta are allowed to continue over long periods, extensive changes will occur in the aortic wall both proximal and distal to the stricture and in branches of the aorta in the vicinity of the stricture.

Aneurysms were present distal to the site of stricture in 10 of this series of 124 cases. Usually these aneurysms occurred at the origin of the first or second intercostal artery distal to the stricture. In every case of the entire series, of course, extensive dilatation and enlargement of the intercostal arteries were present just distal to the stricture, but true aneurysms were present in these 10 cases (Fig. 10). In 6 of them, it was possible to resect the aneurysms and perform anastomosis of the aorta successfully; in 4, the size or location of the aneurysms and the changes in the aortic wall in the region of the aneurysms precluded successful resection and anastomosis. Aneurysms were proximal to the stricture in 2 cases; resection was not possible in these cases. In an additional case, in which a stricture was present between the origins of the left carotid and subclavian arteries, 2 aneurysms occurred distal to the stricture. Resection of these aneurysms and anastomosis were accomplished successfully (Fig. 11). In 1 patient who had an inoperable aneurysm, the site of stricture was not determined.

The degree of gross change in the wall of the aorta above and below the site of stricture and other evidence of degenerative disease of the aorta and its branches in the vicinity of the stricture as estimated by the surgeon at the time of operation proved to be of considerable interest. In 20 patients, no evidence of any such abnormality was present in the wall of the aorta. Ten of these patients were males and 10 females; the ages of this group varied from 10 weeks to 28 years, averaging 15 years. In 40 patients, only slight or minimal changes were noted in the aortic wall. All but 1 of these patients were less than 27 years of age; their ages ranged from 7 to 38 years, averaging 20 years. In this group were 12 females and 28 males. A moderate degree of vascular damage was noted in 48 patients whose ages ranged from 11 to 43 years, averaging 26.6 years, including 32 males and 16 females.

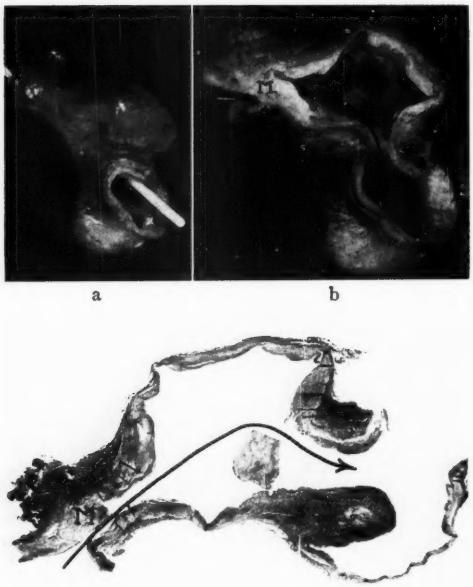

Fig. 11. Segment of aorta removed surgically from a 25 year old woman; specimen viewed from front. The segment had occupied a position between the left common carotid and left subclavian arteries; aneurysms were present between the coarctation and the left subclavian artery. a, External view; the probe lies in the aortic lumen. At the left upper part a tie is seen around a cordlike strand that may have represented an obliterated left vertebral artery arising from the aorta; it was at the level of the coarctation. b, The anterior wall has been removed, exposing the interior of the two aneurysms. *M.*, point of coarctation; *L.S.*, a portion of base of left subclavian artery, which was removed. c, Same specimen oriented in the same way. The coarctation (*M*) is proximal to the two aneurysms. These aneurysms may possibly represent an "incomplete" dissecting aneurysm represented by a break in the intima and media with retraction, leaving only adventitia as the aortic wall in the involved portions (ELVG, ×2.2).

In 16 patients, gross evidence was present of extensive vascular damage with thickened friable aortic walls and plaques; in a few cases, calcification of these plaques was found. In some of these cases, great thinning of the aortic wall and the presence of aneurysms were noted. The ages of the patients in this group varied from 16 to 50 years, averaging 30 years; 12 males and 4 females were included. Only 3 patients who had severe vascular damage were less than 20 years of age; all were males. Nine patients who had severe vascular damage were more than 30 years of age. Only 8 patients less than 21 years of age had moderate vascular damage and only 1 of these was a female.

Thus, it is obvious that the degree of vascular damage to the aorta in the vicinity of the stricture is related directly to the duration of the lesion. The evidence also suggests that males are more likely to undergo severe vascular damage than are females. It appears likely that the more serious damage in males might be related to their vigorous physical exertions with resultant increased strain on the cardiovascular system.

ASSOCIATED ANOMALIES

Other congenital anomalies involving the cardiovascular system were identified in a number of patients who had coarctation of the aorta. A patent ductus arteriosus was found in 16 of the 124 cases in this series; these channels were quite large in 7 of these cases. The presence of a coexistent patent ductus arteriosus was diagnosed definitely before operation in 6 of these latter cases and was suspected in the other. In 2 of these 7 cases, the ductus joined the aorta distal to the stricture, whereas in 5 it was proximal to the stricture. In the other 9 cases, the ductus was quite small and its presence was not suspected preoperatively. A patent ductus with an extremely small lumen may have been present in other cases as well. Since the ligamentum arteriosum usually was ligated both proximally and distally before division, it was not always possible to be sure whether or not a small communication existed between the aorta and pulmonary artery.

The finding of a patent ductus arteriosus in association with coarctation of the aorta, which has not been emphasized in the literature, has occurred more frequently than we had expected. The question has been raised whether the presence of a patent ductus would contraindicate resection and repair of coarctation of the aorta. This has not been our experience. Operation for correction of both lesions was performed successfully in all but 1 of these 16 cases. The ductus arteriosus was divided and the ends sutured in that case. The extent of resection of the aorta that would

have been necessary to remove the stricture and the sutured aortic end of the ductus in this case would have required repair by means of an aortic graft, which was not available; therefore, the coarctation was not disturbed. The aortic stricture in this case, however, was not so marked as in most instances of coarctation. It certainly must be admitted that the presence of a patent ductus arteriosus increases the problems involved in surgical correction of coarctation of the aorta, but it does not prevent or contraindicate operation. The need for operation in these cases is even greater than when coarctation exists alone since the additional hazards of serious occlusive pulmonary vascular changes and right ventricular failure exist in coarctation associated with patent ductus arteriosus.

In 4 cases, a left-sided superior vena cava and an enlarged hemiazygos vein were noted at the time of operation. In 2 cases, as mentioned previously, the left subclavian artery existed only as an obliterated cord, since the stricture of the aorta involved its origin.

One particularly interesting patient had a vascular ring manifested as a double aortic arch. The stricture involved the anterior arch at a point distal to the left subclavian artery but proximal to the junction of the posterior and anterior aortic arches. The posterior aortic arch was about 1.5 centimeters in diameter but was greatly narrowed at its junction with the anterior arch. Operation was accomplished successfully in this case. In a number of instances, the presence of bicuspid aortic valves was suspected but not proved. The presence of other intracardiac defects was suspected occasionally on the basis of clinical findings.

RELATIONSHIP OF LIGAMENTUM ARTERIOSUM OR DUCTUS ARTERIOSUS TO STRICTURE

The ligamentum arteriosum or ductus arteriosus was found in close relation to the site of coarctation in all cases. In 35, it appeared to join the aorta proximal to the stricture. In 69 cases, the attachment was apparently at the site of stricture itself but histologic examination in representative cases usually showed the ligamentum arteriosum to be proximal to the coarctation. In 16 cases, the attachment was slightly distal to the stricture. In 4 cases in which the lesion proved to be inoperable, the relationship of the ligamentum to the site of stricture was not determined. In a number of cases, the aorta was greatly angulated medially by the ligamentum arteriosum.

INTERCOSTAL ARTERIES

It was most unusual in this series of cases to find any blood vessels arising from the segment of aorta between the stricture and the origin of the left subclavian artery. The intercostal and bronchial arteries arising just distal to the stricture almost invariably were greatly enlarged; often they were several times normal size. They were tortuous, thin-walled and extremely friable. The mobilization of these vessels proved to offer the greatest difficulty and danger in the entire procedure. This was particularly true of the right intercostal arteries because of their relatively inaccessible location. In some cases, a sufficient segment of aorta was present between the stricture and the origin of the intercostal arteries to permit resection and anastomosis of the aorta without disturbance of any intercostal vessels. In others, the intercostal vessels immediately below the stricture could be dissected free and occluded by small rubber-covered bulldog clamps while resection and anastomosis were performed. In most cases, it was desirable or necessary to ligate and divide the first two pairs of intercostal arteries arising distal to the stricture, and in many cases bronchial arteries were sacrificed.

SUMMARY

A study has been made of the records in 124 cases of coarctation of the aorta in which surgical exploration has been done at the Mayo Clinic. In 11 (8.8 per cent), the lesion was considered to be inoperable. The lesions in some cases might at present be operable, since aortic grafts are now available.

The series included 42 females and 82 males. The study indicates that the incidence of degenerative changes in the aorta and its branches manifested by intimal fibrotic and atherosclerotic changes in the proximal segment and formation of aneurysms in the distal segment increases with the age of the patient;

these changes are likely to be more severe in males than in females, probably because of increased strain imposed on the cardiovascular system of males.

Coarctation of the aorta usually occurs just distal to the origin of the left subclavian artery but can also occur proximal to this vessel.

Associated anomalies of the cardiovascular system, particularly patent ductus arteriosus, occur frequently but do not necessarily contraindicate or preclude operation for coarctation of the aorta.

Each coarctation of the aorta presents anatomic and pathologic differences that cannot be determined preoperatively in many cases but that affect materially the difficulty and effectiveness of operation.

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ANEURYSMS

AN ABNORMAL dilatation in the course of a blood vessel is progressive because lateral pressure is inversely proportional to the velocity. Arterial and venous enlargements are accompanied by a local reduction in velocity and a consequent increase in lateral pressure. This, in turn, stretches the walls of the vascular channel causing an extension of the dilatation and thereby viciously perpetuating the morbid process.

Arterial expansions are potentially more hazardous than venous because their higher pulsatile pressure leads to destruction and interference with function of adjacent structures and organs and finally their own dissection with rupture and fatal hemorrhage.

The cure of disease begins with prevention and this may be realized in the case of aneurysms when such states as syphilis, arteriosclerosis, and subacute bacterial endocarditis have been controlled. Until then the surgeon must attempt to remove the diseased structure or organ and restore normal function as nearly as possible.

Although aneurysms were obliterated by Antyllus in the third century and aneurysmectomy was advocated by Aetius in the sixth century, successful control of the lesion has only recently been attained. This achievement is due in great measure to a better understanding of the type of aneurysm in relation to its etiology as well as to pathologic changes.

Syphilitic aneurysms are usually saccular with walls of dense fibrous connective tissue sufficiently strong for safe suturing. They contain laminated clot which has been laid down peripherally as the sac dilates. This mechanism diminishes the pressure against the aneurysmal wall because the expansile force is exerted against the neck of the sac rather than its entire circumference. However, the concentrated pounding effect of saccular dilatations in the aorta may lead to erosions of the vertebrae, sternum, and ribs and to interference with function of the trachea, esophagus, heart, and lungs. Rupture of the sac may occur into the pleural cavity, neighboring organs, or to the outside.

Arteriosclerotic aneurysms are fusiform and are commonly encountered, perhaps because of stress, in the lower aorta below the renal arteries and extending to its bifurcation, and in the flexion areas involving the iliofemorals and popliteals. They are associated with extensive calcification, atheromatous and other diffuse vascular changes which cause them to enlarge and become irregularly elongated and tortuous with local points of dilatation and thinning. These changes are not conducive to the destruction of adjacent tissues and organs, and the walls of such dilatations are not as reliable for suturing as the saccular types.

Mycotic or embolic aneurysms are also fusiform. They are due to infected emboli which are dislodged in endocarditis, endoarteritis, and bacteriemias, lodging in smaller vessels otherwise normal, or in small areas of large arteries due to occlusion of the vasa vasorum.

Traumatic aneurysms may be either saccular or fusiform and ordinarily involve normal arteries. They are usually due to a transverse tear of the arterial wall with the formation of a false sac composed of fibrous tissue. However, true aneurysms do occur as a result of blunt trauma permitting an irregular bulge.

Dissecting aneurysms may result from a transverse tear in the intima causing the media to split or from a hematoma in the middle coat of a large artery due to hemorrhage from the vasa vasorum as a result of medionecrosis, leading secondarily to a tear into the intima.

Saccular aneurysms may be treated by extirpation with or without restoration of continuity. The latter is possible in peripheral types because of adequate collateral circulation. Preservation of luminal continuity is accomplished in saccular aneurysms by clamping the wide-mouthed opening, removing the aneurysm, and suturing the defect. Saccules of the aorta may appear on opposite sides, giving the impression of a huge fusiform dilatation. These may be individually removed. When the aneurysm occurs proximal to the left common carotid artery extirpation may not be possible unless the aneurysmal opening can be clamped without preliminary proximal and distal occlusion.

Fusiform aneurysms of the abdominal aorta may be excised with ligation of the inferior mesenteric artery and the area replaced with a preserved homograft or in smaller vessels with an autogenous venograft protected and bolstered by supportive nylon mesh or reactive fibroblastic agents. If such grafts are not available, inert substitutions in the form of plastic materials, nylon web, or lyophilized homografts may be employed. These, like the viable grafts, act as a temporary scaffold enabling the endothelium to line the lumen and fibroblasts to form the wall. It is highly probable that foreign material will be less kindly accepted by the tissues than living grafts, even though the latter are short-lived.

Many problems remain unsolved in the removal of aneurysms. One is the provision for adequate circulation during the process of excision. Interruption of the blood supply for extended periods leads to anoxemia with disturbance of important nerve functions or localized areas of necrosis or even death. This problem may be solved by the use of a bypass to deliver oxygenated blood beyond the point of occlusion or by refrigeration of the entire body so that the metabolic need for oxygen is temporarily decreased. Of course such methods are unnecessary when collateral circulation is ample, as in peripheral aneurysms or those associated with coarctation of the aorta.

Methods of preservation of homografts are at present extremely variable, ranging from quick freezing to no refrigeration and storage in electrolyte solutions, colloid suspensions, alcohol, or human plasma; or drying in vacuum so that a lyophilized graft is obtained. Substitutions for arterial homografts include various elastic materials, fresh or stored fascia or the use of smaller arteries refashioned by longitudinal division and transverse suturing.

After variable periods of time some functioning grafts have become calcified, tortuous, and constricted with proximal and distal aneurysmal dilatations. All observers are agreed that when the aneurysm is severed from its parent vessel it should be removed. Those left in situ have caused degeneration of the graft with subsequent rupture and fatal hemorrhage.

Should aneurysmectomy be unfeasible because of its location, involvement of vital

structures or the general condition of the patient equally good results may be obtained by less radical methods. One of the oldest of these is an attempt to mimic the natural dulling effect of an intraluminal thrombus by inducing clotting through the introduction of wire. In addition to its blunting effect the clot lessens the size of the lumen and probably induces thickening of the aneurysmal wall. At any rate the aneurysm itself becomes smaller, its pulsations less vigorous, and symptoms are relieved.

The wall may be thickened by encasing the aneurysm in reactive materials such as polythene film or plastic sponge or by the injection of fibroblastic agents such as sodium dicetyl phosphate around the adventitia. As the aneurysmal coats become more solid dilatation is inhibited and intraluminal clot seems to form more rapidly.

Thus it now appears that the lethal aneurysm regardless of its position, size, shape, or cause will ultimately yield to the efforts of the surgeon with a good chance that normal physiology will be restored. JACOB K. BERMAN.

SMALL BOWEL OBSTRUCTION IN THE POSTOPERATIVE PATIENT

THE straightforward case of organic small bowel obstruction in the patient who has not had a recent operation and who is not suffering from some preexisting lesion, such as a perforated appendix, is not a very difficult problem. We are all highly conscious of the fact that crampy abdominal pain with vomiting is always intestinal obstruction until proved otherwise, and we all look immediately at the hernial orifices and for old abdominal scars. These cases present the classic signs and symptoms of colicky pain, vomiting, and the gurglings of increased peristaltic activity going on to steadily increasing distention. As the distention progresses, pain gradually recedes and at the same time the sounds of frantically increased peristaltic activity gradually give way to the isolated tinkles, succussion splash, and transmitted heart sounds of the so-called silent, distended abdomen. In the later stages the flat x-ray plate presents the typical ladder pattern of distended small bowel, but at that stage the diagnosis is obvious even to the patient. It is in the very early stages, where there may not yet even be any demonstrable small bowel dilatation, that roentgenography is of great value in diagnosis. The significant point in the x-ray findings of these very early cases of cramps and vomiting is the failure of gas to get through into the colon, so that a flat plate taken 3 or 4 hours after an evacuant enema shows no gas in the cecum, even though the small bowel is not yet significantly distended. This, combined with a persistently negative gastric balance, is evidence enough to support a diagnosis of organic small bowel obstruction.

In intestinal obstruction which does not develop immediately after a laparotomy or as a complication of peritonitis, the really important question is whether it is a simple stenosing or band obstruction, or whether it is the much more dangerous closed loop or strangulating obstruction. The diagnostic features pointing to a strangulating lesion are localized tenderness, the suggestion of a mass, signs of peritoneal irritation, rising leucocyte count and falling hemoglobin estimation in a patient who is becoming acutely ill much more rapidly than most simple obstructions do. X-ray examination is often helpful in the recognition of an obstruction as closed loop in type, as the flat plate will frequently show not only the characteristic ladder pattern of simple small bowel obstruction but also one or more fixed coils of small bowel in which the disten-

tion is very much more marked. These more distended loops usually occur at the site of the localized tenderness and the vague mass.

In the postoperative patient, simple paralytic ileus is no longer a serious matter provided it is recognized and treated early. The difficulty is that almost every postoperative patient, whose operation has entailed the opening of the peritoneal cavity, shows some signs of intestinal disturbance within the first 3 postoperative days in the form of vomiting, distention, or simple gas pains. Although the great majority of these minor disturbances subside within a few days on simple measures, a few progress until the patient becomes seriously ill from the biochemical disturbances which result from prolonged distention. For this reason it is highly important to treat every patient who has had major abdominal surgery, or who has peritonitis from any cause, as though we knew that he would become one of the unlucky few. Intubating these patients preoperatively or immediately after operation, and applying continuous suction to the intestinal decompressing tube, will prevent adynamic ileus.

Our biggest worry in the postoperative patient with distention, vomiting, and failure to pass flatus is whether his obstruction may be due to an organic lesion rather than to simple paralytic ileus. The physical findings in an abdomen are changed by a recent wound in its wall. Tenderness of the wound may mask deep tenderness and the resistance of the musculature is often absent postoperatively. Here again x-ray examination is helpful. In distention due to ileus the flat plate will usually show generalized dilatation of the intestine involving the colon as well as the small bowel. In organic small bowel obstruction, it is the small intestine only which is distended, and the colon will not be dilated and will contain little or no gas. We have found, however, that it is not safe to rely on the x-ray evidence alone, as this may sometimes be misleading. Of much greater clinical value is the patient's response to intestinal decompression and what happens to his gastric fluid balance after intubation with an intestinal decompression tube to which continuous suction is applied.

The approximate distance from the patient's nostril to his pylorus is estimated and this distance is marked on a long intestinal tube such as the Harris tube. If the patient is not too ill, he may be assisted to sit up to facilitate the passage of the tube through his nostril, pharynx, and esophagus into his stomach to the distance already marked on the tube. The head of the bed is now flattened completely, and the patient is made to lie well over on his right side for a few hours, during which he is allowed clear fluids by mouth. If he has been vomiting large quantities, the stomach should be emptied by syringe aspiration and continuous suction should be applied to the tube immediately in order to lessen the likelihood of vomiting which might bring up the tube.

There are several indications that a tube has passed through the pylorus into the duodenum. The character of the aspirated fluid usually changes from the clear fluid of gastric content, often recognizable as something recently drunk, to the darker, more viscid, more bile stained fluid of duodenal content. Moreover, if the patient is given something to drink and the same fluid is immediately recovered from the tube, the tube is probably still in the stomach. If, however, there is a delay of some minutes and then the fluid recovered is not so easily recognizable, the tube has probably passed into the duodenum. The suspected position of the tube in the duodenum must be definitely confirmed by a portable x-ray machine before one starts advancing it an inch an hour to allow

it to pass on down the small intestine and empty the bowel as it goes.

To maintain continuous soft suction on the intestinal content at the end of the tube, a Wangensteen suction apparatus is very useful. Because of the frequency with which the intestinal tube becomes plugged, however, it is imperative that the indwelling tube be disconnected from the Wangensteen apparatus at least every 2 hours to irrigate the indwelling tube and make sure its lumen is clear, to empty the bowel of all fluid content that can be syringe aspirated then, and to connect the Wangensteen apparatus again and make sure it is running without air traps or leaks.

The nursing of a patient on gastrointestinal suction is an exacting task requiring intelligence, patience, training, and constant attention to detail. Not only must the indwelling tube be kept clear and the suction running smoothly and effectively, but also the exact quantities of fluid aspirated must be carefully charted as well as every drop the patient drinks and every ounce of urine he excretes. The exact quantity and kind of fluids given intravenously must also be accurately recorded, to maintain electrolyte and water balance by correctly assessing the patient's needs from one 8 hour period to the next.

On such a regimen we have found that the most valuable and reliable distinguishing point between the patient with simple ileus and the patient with organic obstruction is the progressive status of his gastric balance. In paralytic ileus, within 24 hours of the tube passing through the pylorus, it will be found that the patient is drinking more than can be recovered from the tube, that is that his gastric balance is becoming positive. Moreover, his distention will be markedly reduced and he often starts to pass flatus per rectum. In organic obstruction, the patient's condition may be tremendously improved by the reduction of his distention by continuous intestinal suction, and the correction of his dehydration and replacement of his electrolyte losses by the intravenous administration of the right repair solutions. But he is still losing far more fluid by the intestinal tube than he is taking by mouth; that is, his gastric balance is still strongly negative. Operation is essential to relieve his obstruction before electrolyte and fluid losses become irreplaceable.

The distinction between organic obstruction and paralytic ileus in the distended, vomiting postoperative patient is of the greatest importance. The added insult of reopening the abdomen of a patient who is suffering only from adynamic ileus may so aggravate his condition as to make his intestinal atony irreversible and ultimately fatal. On the other hand, failure to operate upon the patient with organic obstruction to relieve that obstruction may be equally fatal. The x-ray examination is not an infallible guide. With the aid of the fluoroscope if need be, it is almost always possible, even in the most severely distended patient, to get a long intestinal decompressing tube through the pylorus and into the upper small bowel within a few hours. If, after 24 hours of continuous intestinal suction, such a patient is still losing a great volume more fluid by his intestinal suction than he is able to take in by mouth, it must be assumed that his obstruction is organic and persistent and will only be relieved by operative interference. In contrast it will be found that 24 hours of effective intestinal suction in the patient with simple adynamic ileus will not only correct his distention, but will so restore the peristaltic activity of the small bowel that one can no longer recover from the tube a volume of fluid equal to that which the patient is drinking. The importance of the nursing care cannot be overestimated. JESSIE GRAY.

THE SURGEON AT WORK

SURGICAL PATHOLOGY OF THE COLONIC STOMA

GUY L. KRATZER, M.D., F.A.C.S., Allentown, Pennsylvania

ALTHOUGH rare, the colonic stoma is subject to certain complications, which may develop in spite of all precautions taken to prevent them. This study is a didactic review of the pathologic conditions occurring in the colonic stoma as observed at our hospital or recorded by others. An attempt is made to offer an opinion as to the major cause of each entity and, similarly, to suggest its prevention or cure.

The colonic stoma may be either single or double barrelled. Single barrelled colostomy is established by transecting the bowel and bringing the proximal end out through the abdominal wall or to the perineum. Double barrelled colostomy is established by bringing a loop of bowel out on the abdominal wall and opening it at the proper time. De Martel clamp and glass rod are used respectively.

From the Department of Proctology, Allentown Hospital, Allentown, Pennsylvania.

Neoplastic and the ordinary inflammatory lesions as seen elsewhere in the bowel are not peculiar to the colonic stoma and will not be considered here.

Retraction of the colonic stoma is usually due to the early removal of the retaining clamp or other support, before healing has taken place, or to insufficient mobilization of the bowel. The bowel, if it is to be a single barrel colonic stoma, should extend for a distance of at least 1½ inches above the skin surface without undue tension and be held in that position by a clamp for at least 8 days. If a loop colostomy is planned, such position should be maintained for a period of at least 2 weeks. The colonic stoma may be opened with cautery without disturbing the clamp or glass rod anytime after 4 hours following surgery as the peritoneal cavity is sealed off by this time. The average colonic stoma, however, will not need opening before the end of 48 hours. The wound is

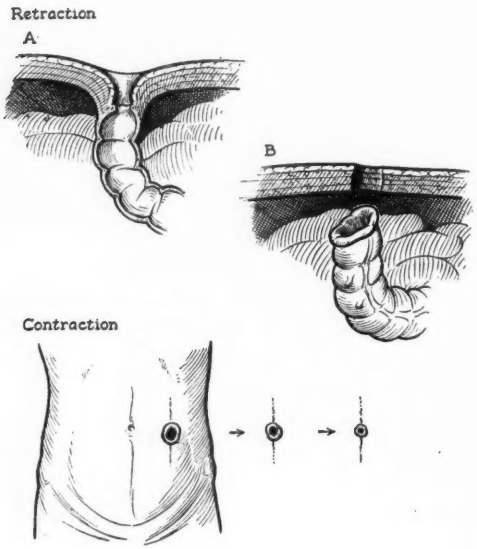

Fig. 1.

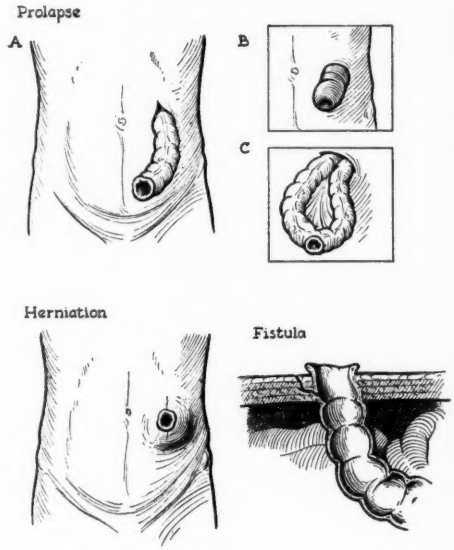

Fig. 2.

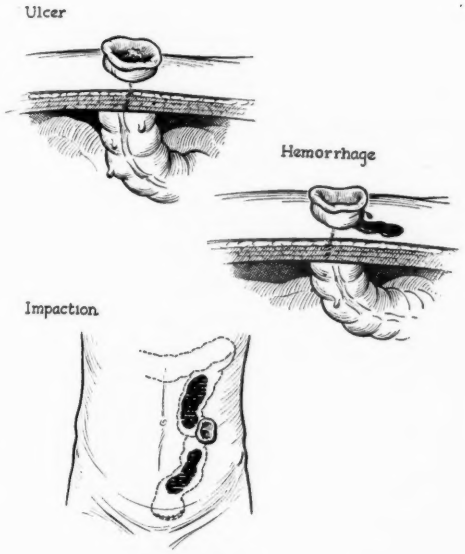

Fig. 3.

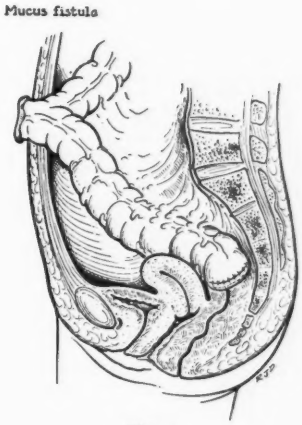

Fig. 4.

well protected with vaseline gauze. Actual stool is rarely expelled before the end of 4 or 5 days and accounts for the low incidence of wound infection. Mineral oil by mouth is used if necessary. Irrigations are not used until the wound is healed. The wound is exposed to light and air twice daily. Diarrhea, which makes cleansing more difficult and predisposes the wound to infection, is controlled by the use of aspirin or paregoric. More recently sulfathalidine has been used as a routine measure. If the patient is seen after retraction has taken place, usually several weeks or months after operation, a minor plastic procedure to elevate the bowel is necessary. The bowel is freed from the abdominal wall and again elevated above the skin surface with clamp or glass rod, as the case may be. The rare case of retraction and complete separation from the abdominal wall immediately following surgery requires emergency surgery to prevent infection of the peritoneal cavity. An inadequate clamp or displaced glass rod would account for such a situation.

Contraction of the colonic stoma is prevented by adequate opening of the bowel, frequent dilatations for a period of at least 3 months following colostomy, and occasional inspection for several years thereafter. However, dilatation is not necessary during the first week. After contraction has occurred, the fibrous skin band responsible for it may be severed as an office procedure and followed with dilatations as indicated.

Prolapse of one or more coats of the bowel, constituting a colonic stoma, is predominately a complication of double barrelled colostomy. One may usually prevent such a development by bringing out the loop of bowel in such a manner as to have the proximal limb under slight tension. This procedure is admittedly difficult in performance of transversostomy because of the mobility of this segment of colon. Appliances used for collecting

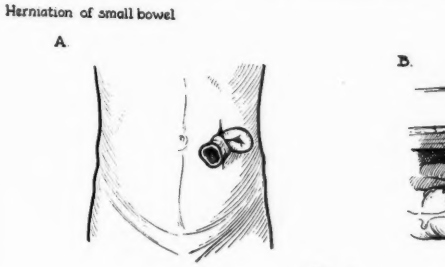

Fig. 5.

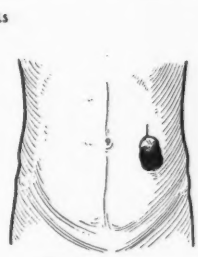

Fig. 6.

the bowel discharges will tend to produce prolapse because of the vacuum created. Mild prolapse should not cause concern. The more severe type, with danger of torsion and strangulation, must be treated surgically. Simple circular amputation of the mucosa followed with interrupted sutures may suffice. Severe cases require transection of the bowel.

Herniation of the muscles immediately surrounding a colonic stoma frequently follows wound infection, unphysiologic incisions, and operations on those patients with inherently weak abdominal walls or with general obesity. This complication may largely be avoided by bringing the bowel selected for stoma out through a separate small muscle-splitting incision. The wound need only be large enough to admit the bowel without danger of strangulation. Repair, if justified, is accomplished as in any incisional hernia. Otherwise an abdominal support is used.

Fistula means that seepage of infective material from the bowel to the wound has occurred. Superficial fistulous tracts if they do not close spontaneously may be managed similarly to those at the anus. The deeper ones require that the involved bowel be transected and the mobilized segment brought out, just as accomplished in the original operation. It is important to avoid placing stitches in the bowel wall and to avoid insertion of catheters, finger manipulation, or other trauma early in the postoperative course.

Ulceration and hemorrhage occur infrequently, usually, as a result of trauma. These complications may largely be avoided by placing the stoma in such a manner as to facilitate fitting an appliance. Bleeding is controlled by ligation. Irritation from ill-fitting appliances should be avoided.

Fecal impaction is more apt to occur in double barrelled colonic stoma. Diagnosis is made by digital examination. It may be prevented by proper attention to bowel hygiene and treated by irrigation or mineral oil instillation.

Mucous or fecal fistula, occurring in the posterior wound, is occasionally observed following the establishment of a sigmoidal loop colostomy and posterior resection of the rectum. This type of operation results in the formation of a blind end of sigmoid which is allowed to remain in the pelvis. In most instances healing is spontaneous. In a few, associated retraction of the colonic stoma is found. In these cases surgical elevation of the colonic stoma will frequently result in healing.

Herniation of a loop of small bowel along the side of the colonic stoma is another rare complication. The space between the abdominal wall and bowel should be exactly large enough to admit the tip of the index finger. Deviation from this rule is dangerous practice. Abdominal support supplemented with adhesive straps is essential during the immediate postoperative period for prevention of this complication. Immediate minimal surgery, preferably under local anesthesia, with packing and pressure bandages when feasible, is the only recourse after such a complication has occurred.

Intestinal obstruction requiring immediate laparotomy may be precipitated by a loop of small bowel caught in the space between the colonic stoma and the parietal peritoneum. This is more apt to occur when the colonic stoma is brought out through a separate wound in the left lower quadrant because the space is smaller. To avoid this complication it is necessary to close this area at the time of surgery.

Necrosis of a portion or all of the bowel used as a colonic stoma may occur because of deficient blood supply or constriction at the abdominal wall. If necrosis extends proximally beyond the skin level, the incision must be reopened, and enough viable bowel should be mobilized to serve as the stoma.

CONCLUSIONS

The colonic stoma is subject to certain immediate and long range complications. A program of long range care should be adopted.

The illustrations (Figs. 1 to 6, inclusive) are self-explanatory.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE 150 page monograph, *Effective Inhalation Therapy*[1] by Dr. Edward Rayner Levine, is designed to acquaint the busy clinician with the latest methods of the effective use of various forms of therapeutic gases in disease. The first portion of the text reviews in simplified form the physiology of respiration. This discussion is illustrated by numerous colored Disney-like diagrams which adequately present the physiology of respiration in both health and disease.

Next the author differentiates the use of oxygen in those disease states which cause acute oxygen want from those in which there is chronic anoxia. The chapter on chronic anoxia is particularly well written because it clarifies the technique of oxygen therapy in such chronic diseases as heart disease, asthma, and emphysema, and differentiates the use of oxygen in acute asphyxia from chronic anoxia.

Because the author has tried to divide the book into sections dealing with physiologic anoxia as well as the use of inhalation therapy in specific disease there is a certain amount of repetition.

The chapters dealing with the fundamental use of inhalation therapy for symptoms such as chronic cough, hiccup, intermittent dyspnea, and acute asthma are helpful.

The title of the book is a little misleading because over 90 per cent of the text discusses the use of oxygen, and the use of such gases as carbon dioxide and helium are mentioned only incidentally. The discussion of use of aerosol is not up-to-date.

A review of the technique and the use of inhalation therapy by catheter, positive pressure mask, or tent should be extremely helpful to the doctor who prescribes it daily as well as to the house staff and nurse who are constantly supervising its use. For a simple, well illustrated, quick review of present day inhalation therapy this book may be recommended.

HOWARD A. LINDBERG.

THE aim of the author of the 481 page volume *Klinische Fehldiagnosen*[2] is to point out and discuss the weak points in differential diagnosis which are the causes of common mistakes. The major part of the book deals with problems of internal medicine including the diseases of children; another part, however, is concerned with general surgery and gynecology. Special chapters deal with liver diseases, gastrointestinal disorders, nerve diseases, and endocrinology.

Well described case histories, in all 170, and the majority of them from the author's personal experience form the basis for the discussion. In several of them the key to the diagnosis was found first at autopsy. These case histories are very instructive and contain a wealth of valuable material. Some clinical questions such as the role of focal infection in rheumatic diseases and the clinical evaluation of liver function tests are discussed in detail. Each chapter ends with a brief summary. The author states that very often the missed opportunity for an early diagnosis is to be regarded from the patient's point of view as a faulty diagnosis.

This book contains so much material that a more detailed review is impossible. There are, of course, statements with which many will not entirely agree. A surgeon would say perhaps that the diagnostic aim in the presence of appendicitis is not to make a correct diagnosis in as high a percentage of cases as possible, but rather to determine in the individual case whether or not exploratory laparotomy could safely be avoided. Some would feel that rheumatoid arthritis should now be regarded as a metabolic disorder and not as an infectious disease.

The character of the book is such that it demands thorough study rather than being adapted to the busy work of the wards.

Illustrations, diagrams, and drawings are very good and instructive. The bibliography gives many references of value with surprisingly few omissions, but only to contributions in the German language.

ERIK MOBERG.

THE book entitled *The Treatment and Classification of Cancer*[3] is a provocative little book. Those who were present at the second National Cancer Conference at Cincinnati in 1952 may remember the animated discussion provoked by Dr. J. C. Lees's somewhat unorthodox views on the treatment of breast cancer. His thesis had previously been presented jointly with Dr. W. W. Park in a paper in this Journal (1951, 93: 129–152) on "The Absolute Curability of Cancer of the Breast." In brief, Park and Lees were not convinced that earlier diagnosis and treatment of breast cancer resulted in a higher cure rate. The present work reaffirms and extends

[1] EFFECTIVE INHALATION THERAPY. By Edwin Rayner Levine, M.D. With the co-operation of Alvan L. Barach, M.D., J. Winthrop Peabody, M.D., and Maurice S. Segal, M.D. 159 pages, illustrated. $4.50. Chicago: National Cylinder Gas Co., Medical Division, 1953.

[2] KLINISCHE FEHLDIAGNOSEN. By Prof. Dr. M. Bürger. 481 pages, illustrated. Stuttgart: Georg Thieme, 1953.

[3] THE TREATMENT AND CLASSIFICATION OF CANCER. By James C. Lees and Thomas W. Lees. 63 pages, tables and diagrams. Edinburgh: Oliver & Boyd, Ltd., 1952.

this belief with reference to cancer in general. The first part of the book is an enquiry into the "absolute curability of cancer" and it is concluded "that there is not sufficient evidence for the dogma that excision of the primary tumor sometimes prevents distant metastatic spread." The bearing this conclusion has on the conventional theory of cancer behavior is discussed and some modifications of the principles of cancer treatment are suggested.

The book finishes with a long section on "Cancer Nomenclature" in which a new provisional classification of cancer is suggested. The final part of this section deals with a discussion of "Evidence in Cancer."

There would seem much of value in this book in that the views expressed are likely to cause much argument; this is admirable if fresh knowledge accrues from such discussion. But the reader will find much that may annoy. For example, one may doubt the authors when they say, "No one can say where the cause and cure of cancer will be found, but at least it can be said with assurance that the most likely place left now to find it is where it has never really been sought—in the cancerous individual himself." Again, "Much has been learned of the behaviour of induced and transplanted tumours in animals from the immense amount of animal and 'pure' cancer research—but hardly a single item which adds to the understanding of the cause, behaviour and cure of human cancer."

L. R. C. AGNEW.

AFTER indulging in an incongruous but perhaps required obeisance to the rulers of East Germany, the author of the monograph entitled *Kolpofotogramme; zur Enfuehrung in die Kolposkopie*[1] discusses the development and use of a special photographic technique whereby colposcopic observations can be precisely and permanently recorded.

The apparatus is described and illustrated. Seventy-three photographs are presented in atlas form to illustrate the multiform variations seen in benign conditions of the mucosa of the portio of the cervix. A second volume is planned to illustrate pathologic conditions.

The author observes that colposcopy has been proved by Hinselmann to be an essential procedure in the detection of early cancer of the portio. Mastery of colposcopy has remained limited to a relative few, however, because of the difficulty of correct interpretation of individual observations. It is proposed that this difficulty can be overcome by study of many photographic reproductions such as those presented in the present volume. In addition, serial photographs of an individual patient under study can be made.

The photographs in this volume are precise in detail and a wide range of mucosal alterations are sharply illustrated. This monograph should be of considerable value to those who wish to familiarize themselves with the colposcopic appearance of the portio of the cervix.

FRANK M. MAHER.

[1]KOLPOFOTOGRAMME; ZUR ENFUEHRUNG IN DIE KOLPOSKOPIE. By Dr. Med. Robert Ganse. Vol. 1. Berlin: Akademie-Verlag, 1953.

THE author of *Heart and Circulation*[2] has written a brief text on the subject for the general practitioner and medical student. No effort is made to discuss the material in great detail, consequently the book will prove inadequate for the profoundly interested student. In spite of his brevity Dr. Sclar covers the field of cardiovascular diseases remarkably well.

The book is well presented and the illustrations are, for the most part, effective. This small volume will appeal to the general practitioner to whom it may be recommended.

JOHN A. MART.

A SMALL, well illustrated monograph presenting the details of the management of thoracic surgical patients has been written by Belcher and Grant,[3] former resident surgical officers at the Brompton Hospital in London. They have succeeded very well in their attempt to instruct members of the medical profession who are less informed about the minor procedures and routines used in the diagnosis and preoperative and postoperative care of such patients.

The chapter on general principles contains some pertinent and significant facts about the mechanics of the bronchi and pleura. Indications and complications are given for artificial pneumothorax and pneumoperitoneum, and bronchoscopy, as well as their technique. Empyema, acute and chronic, is adequately treated in brief expositions. The management of patients with bronchiectasis, bronchogenic carcinoma, mediastinal tumors and cysts, "coin" lesions and myasthenia gravis is outlined well. The principles in the treatment of lesions of the heart, pericardium, great vessels, esophagus, and diaphragm are discussed. Essential hypertension, spontaneous pneumothorax, and pulmonary tuberculosis are briefly presented from the surgical point of view.

This small book should be carefully read by members of the house staff of general and specialized hospitals, and all others, who have the immediate responsibility for the care of thoracic surgical patients.

EARL B. SANBORN.

THE book entitled *Diseases of Muscle; a Study in Pathology*[4] is the first treatise in England on this wide and important subject. A conspicuous gap in

[2]HEART AND CIRCULATION; DIAGNOSIS AND TREATMENT. By Meyer Sclar, M.D., F.A.C.C. 358 pages, illustrated. $7.50. New York: Froben Press, Inc., 1953.

[3]THORACIC SURGICAL MANAGEMENT. By J. R. Belcher, M.S., F.R.C.S., and I. W. B. Grant, M.B., M.R.C.P.(Edin.). Foreword by Sir Clement Price Thomas, K.C.V.O., F.R.C.S. 196 pages, with 65 illustrations. $3.50. London: Baillière, Tindall and Cox; Baltimore: The Williams & Wilkins Co., 1953.

[4]DISEASES OF MUSCLE; A STUDY IN PATHOLOGY. By Raymond D. Adams, M.A., M.D., D. Denny-Brown, M.D., D.Phil., F.R.C.P., and Carl M. Pearson, M.D. 556 pages, with 347 illustrations. $16.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1953.

the literature has been filled in a most creditable manner. Written mainly from a pathologic standpoint, the text covers every conceivable aspect of diseases affecting the muscles.

The opening chapters are devoted to a detailed account of the physiology and histology of normal muscle, adequately illustrated by numerous well reproduced photomicrographs in black and white. Next the authors consider the various pathologic processes as they affect muscular tissue.

Against this background they then give a detailed description of all aspects of muscular disease, both surgical and medical. Naturally more stress is laid on the medical and neurologic disorders.

As previously mentioned, the numerous photomicrographs are particularly valuable and the work certainly fulfills its claim to be a complete modern treatise of muscle pathology.

Though mainly useful to neurologists and pathologists, this book, with its very complete bibliography will remain a standard reference work for all who are called upon to diagnose and treat these uncommon disorders. HAROLD BOLTON.

THE atlas of 205 pages entitled *Tumors of Bone; a Roentgenographic Atlas*[1] consists of reproductions of roentgenograms of tumors and other disorders of bone. The descriptive captions are rather long and include some general discussion. The first chapter of 29 pages is on osteogenic sarcoma which the authors separate into lytic and osteoblastic type. Chapter 2 on chondrosarcoma has excellent examples of the variety of forms which this neoplasm may assume. The sections on Ewing's tumor and reticulum cell sarcoma are perhaps the best part of the atlas. A short chapter on myeloma gives its more typical roentgenographic findings. Metastatic carcinoma is covered quite adequately. Chapter 9 on benign tumors includes all the usual examples. One might disagree with the inclusion of the periosteal osteoma under benign tumors since this has been shown to be a malignant neoplasm. Also, the consideration of fibrous dysplasia, bone cyst and osteoid osteoma as neoplastic diseases is questionable. The term "periosteal giant cell tumor of the shaft of the femur" (Figs. 120 and 121) is an unfortunate one as the disorder pictured here is considered by most to represent an angiomatous neoplasm unrelated to giant cell tumor. The last section on "Non-Neoplastic Conditions of Bone Simulating Bone Tumors" occupies over one quarter of the text. This includes infections, metabolic and circulatory disorders amongst other diseases of the skeleton. The book might, therefore appropriately bear the title "Roentgenographic Atlas of Skeletal Diseases." A subject index concludes the book. The roentgenographic reproductions in general are satisfactory.

[1]ANNALS OF ROENTGENOLOGY. A SERIES OF MONOGRAPHIC ATLASES. Vol. 21. TUMORS OF BONE; A ROENTGENOGRAPHIC ATLAS. By Bradley L. Coley, M.D., F.A.C.S., and Norman L. Higinbotham, M.D., C.M., F.A.C.S. 216 pages, with 172 illustrations. $10.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1953.

This volume will be of particular interest to those desiring a ready review of roentgenographic characteristics of bone tumors. C. HOWARD HATCHER.

THE volume entitled *The Surgery of Infancy and Childhood*[2] by Dr. Gross of Boston, who since the retirement of William E. Ladd has become recognized as the leading pediatrics surgeon in this country, is unquestionably the outstanding work in children's surgery that has thus far been published. While, as the title implies, it is concerned chiefly with principles and techniques, in reality it goes far beyond these limitations and presents in great detail follow-up studies and late results of treatment over a period of some 20 years. To be sure, Dr. Ladd, during his active life as Chief of the Surgical Service at the Children's Hospital, had much to do with the accumulation of the enormous material from which the data have been obtained, but this book is largely the result of the efforts of Dr. Gross himself. It is the product of his own pen, and its value to a great extent lies in his own interpretations of the evidence presented and his own conclusions concerning the value of methods of treatment. Moreover, in several fields included in this volume, i.e., surgery of the patent ductus arteriosus and coarctation of the aorta, Dr. Gross' original investigations contributed greatly to the success of the now well recognized methods of treatment.

The scope of subjects covered is very wide. Beginning with preliminary remarks about the field of so-called "Pediatric Surgery," the author takes up preoperative and postoperative care, especially of premature babies, and thereafter in 68 chapters presents a complete discussion of all phases of abdominal, thoracic, cervical, and genitourinary surgery, with particular emphasis on tumors, and the new developments in the rapidly expanding field of surgery of the heart and great vessels. In the discussion of every subject the author presents the clinical symptoms, the pathology, the diagnosis, and the reasons for the methods of treatment employed at the Children's Hospital. This is followed in each instance by a long term follow-up study and a summary of late results, and at the close there is a brief but well selected bibliography.

It is a large volume. It contains approximately 1,000 pages with 1,488 illustrations. The photography is excellent and the drawings of the artist Etta Piotti are simple, accurate, and clear cut. It is not intended to be a complete textbook covering all phases of surgery as applied to children, inasmuch as it deals not at all with neurosurgery and barely mentions problems involving bone and fractures. Its purpose is rather the presentation of the material which has come through the general surgical service at the Children's Hospital, and, as the author says in his preliminary remarks, it contains "only those

[2]THE SURGERY OF INFANCY AND CHILDHOOD; ITS PRINCIPLES AND TECHNIQUES. By Robert E. Gross, M.D., D.Sc. 1,000 pages, with 1,488 illustrations. $16.00. Philadelphia, London: W. B. Saunders Co., 1953.

chapters which might be of widest interest and greatest help to other students and physicians."

It is a privilege to review this excellent book, and I strongly urge that it become a part of the active library of all students of medicine, of all pediatricians, and especially of all surgeons whose field of work has to do with infants and children.

EDWIN M. MILLER.

THE book *Surgery of the Pancreas*[1] by Cattell and Warren contains 374 pages with 100 illustrations and many tables. In this excellent and practical discussion of surgical lesions of the pancreas, the authors present not only the accumulated experience of the Lahey Clinic but their own personal views. The anatomy and physiology of the pancreas are reviewed, but main emphasis is given to diagnosis, clinical management, and surgical treatment of various surgical conditions of the pancreas. These include congenital malformations, such as aberrant and annular pancreas, acute and chronic relapsing pancreatitis with its various complications, injuries of the pancreas, hyperinsulinism and carcinoma of the head of the pancreas and periampullary region. One chapter reviews both the personal experience of the authors and other surgeons with total pancreatectomy. Details of surgical technique for resection of the head of the pancreas (Whipple operation) are reported in some detail. Most other surgical procedures are discussed in a more general manner, which is entirely adequate for the surgeon of some experience.

Definite opinions are expressed on controversial subjects. For example, the authors advocate marsupialization rather than internal drainage for the usual pseudocyst of the pancreas; resection of the head of the pancreas is advocated in many cases of advanced chronic, recurring pancreatitis associated with calculi in the distal portions of the pancreatic ducts, and direct mucosa-to-mucosa anastomosis between the duct of Wirsung, and the jejunum is advised in performing the Whipple operation, with suture of the remaining end of the pancreas, rather than imbedding the entire cut end of the pancreas into the jejunum. Prevention and treatment of injuries of the pancreas, especially the pancreatic ducts, as may occur occasionally in operations for lesions which are primary in the stomach or duodenum, are discussed in an enlightening and practical manner. Detailed case reports are liberally employed to illustrate significant points in diagnosis and management.

The unusually large experience of the authors makes this book a valuable reference on surgical diagnosis and treatment of the unusual as well as the more common pancreatic lesions. The authors rightly state that surgery of the pancreas is a relatively new field in which not many surgeons have had the opportunity for extensive experience over a period of years and that current opinions may be modified in the future. Bibliographic references are numerous and include all major contributions to the field.

JAMES T. PRIESTLEY.

IN THE enlarged and revised second edition of the already familiar work by Moseley entitled *Shoulder Lesions*,[2] there are added two valuable chapters on the neurologic aspects of shoulder lesions and an x-ray diagnosis and treatment, contributed by Dr. Moseley's specialist colleagues.

The author has had a special interest in lesions around the shoulder. A long experience enables him to offer a logical approach to the treatment of these conditions. His views on ruptures of the rotator cuff are now familiar from his previous monograph on the subject.

In the operative treatment of recurrent dislocation, Dr. Moseley favors a Bankart type of repair, and advocates the use of a metallic glenoid rim in cases in which the bony rim is deficient. He has applied this in 10 cases with success in all. This variant of the anterior bone block is a new departure, on which judgment must be reserved.

A conservative attitude, with early active exercises, is emphasized in the treatment of most fractures around the upper end of the humerus, especially in the older patients. This is practice with which most will agree.

The chapter on fibrositis around the shoulder is the most controversial in the book, containing as it does somewhat debatable statements regarding the causation and treatment of this highly speculative condition.

The author holds out hope that cortisone will play an important role in the treatment of the stiff and painful shoulder. Up to date, the general impression from most controlled series where this drug has been used is that it has not proved as helpful in such cases as had been hoped.

The amount of space devoted to illustrations is much larger than usual in a book of this size, and the numerous and lavish colored drawings by Helen MacArthur and Frank Netter form a striking content of the book.

In addition, drawings and x-ray reproductions are of a high standard. A comprehensive bibliography at the end of each chapter makes the book valuable from a reference point of view.

This is a useful book, written mainly from a clinical standpoint, which, as a pictorial atlas of shoulder affections, will command a place for itself in the library of many orthopedic surgeons.

HAROLD BOLTON.

IN ADDITION to being a qualified and experienced orthopedic surgeon the author of *Man's Back*[3] has made a long and thorough study of the

[1] SURGERY OF THE PANCREAS. By Richard B. Cattell, M.D., and Kenneth W. Warren, M.D. 374 pages, with 100 illustrations. $10.00. Philadelphia and London: W. B. Saunders Co., 1953.

[2] SHOULDER LESIONS. By H. F. Moseley, M.A., D.M., M.Ch. (Oxon.), F.R.C.S. (Eng. & Can.), F.A.C.S. 2nd rev. enl. ed. 329 pages, with 216 illustrations. $12.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1953.

[3] MAN'S BACK. By Theodore A. Willis, M.D., F.A.C.S. 161 pages, with 125 illustrations. $9.50. Springfield, Ill.: Charles C Thomas, 1953.

defects in the structure of the laminae of the lumbar vertebra with a large amount of anatomic material for his investigation. This is a monograph on the human back starting with the embryology and covering the various congenital dysplasias, diseases, injuries, and tumors that occur in the back.

The author points out that periodically new discoveries have occurred particularly with the perfection of roentgen technique, and that each time there was a new discovery its importance was overemphasized. After a period of time the emphasis decreased until it was below the true, actual value. It is the author's purpose to present the discoveries and clinical findings in their proper perspective on the basis of his experience.

The subject matter includes embryology, anatomy, proper examination of the back, injuries, diseases, tumors, and a chapter on scoliosis. There is also a chapter on physical therapy for back lesions as well as one on operations.

The illustrations are excellent, particularly those showing anatomic lesions in the lumbar area.

The author recognizes functional inadequacies of the structures, bones, ligaments, and muscles as a predisposing factor to strains and sprains. Weakness and fatigue of the structures increase susceptibility to injury and delay recovery following injury. He recognizes the relation between postural deformities and general debility resulting from improper nutrition, lack of exercise, mental depression, and prolonged strain. These postural faults he lists as kyphosis, lordosis, and scoliosis. In dealing with scoliosis per se he still speaks of the large group of scoliosis as being idiopathic in type.

This is an excellent monograph on the back, covering the generally accepted present knowledge, and it coincides with the generally accepted concepts.

EMIL HAUSER.

IN THE volume entitled *Modern Concepts of Medicine*[1] the author attempts to present newer concepts of medicine which have developed in medical thinking since Hans Selye first advanced his theory of stress and adaptation. He believes medicine should no longer be bound by traditional thought but should be interpreted in the light of normal and deranged cellular physiology.

In addition to Selye's theory, this author advocates the field of cybernetics which, when applied to medicine, means that all body functions are controlled by definite regulatory mechanisms. Cybernetics is a theory applicable also to the fields of chemistry, physics, and engineering. After outlining these theories, he writes an abbreviated textbook of medicine but fails to correlate these newer theories with standard classification and description of disease.

Although the theories of stress, adaptation and cybernetics are interesting, the author does not convince us that it is time to revolutionize medical thought for theories not yet proved or accepted. The book was not well conceived or presented. For practical purposes it could be used as another handbook of medicine.

HOWARD A. LINDBERG.

A FORMER student of Hochenegg, Felix Mandl has long been interested in paravertebral sympathetic blocks for diagnostic and therapeutic purposes. His classic monograph on diagnostic paravertebral blocks, with which he relieved segmental visceral pain at various levels appeared in 1926 and serves as the foundation of many of our present well established procedures. In the present monograph *Blockade und Chirurgie des Sympathicus*[2] he extends his studies to sympathectomies and tries to establish clear-cut indications for the chemical block as against surgical excision of the ganglionated chain.

After a brief but inclusive historical sketch, the anatomy and physiology of sympathetic interruption are described. No discussion is given of the controversial problem of muscle-circulation versus cutaneous blood flow after sympathectomy, but generally speaking, the literature is admirably covered and the American surgeon will find a host of interesting continental references.

The approach to the indications and results of sympathetic blocks and sympathectomies is refreshingly clear and the author's opinions are based on a critical study of the literature and his considerable personal experience, which dates back over 30 years. Animal experiments are not cited nor are hasty conclusions drawn from a few artificially set and poorly designed animal experiments which so easily permeate the present literary field. As Professor Burn once said, "The physiology of the sympathetic nervous system would have to be rewritten if the hare were substituted for the cat."

There may be certain areas which the author, who has only recently returned to his native city from a period of exile, could not have completely covered. In the chapter on megacolon, the work of Swenson is unmentioned; nor does he stress the value of high lumbar sympathectomies including the eleventh or twelfth dorsal ganglion in causalgia, although he quotes Mayfield's work. Nevertheless, this monograph should be read with absorbing interest by surgeons interested in the sympathetic nervous system. The printing and illustrations are excellent and the bibliography is most complete.

GEZA DE TAKATS.

THE very formidable and ambitious undertaking, *The Book of Health*,[3] which "tells what 242 doctors believe you and your family should know about

[1] MODERN CONCEPTS OF MEDICINE. By Julius Jensen, Ph.D. (Med.), M.R.C.S. (Eng.), L.R.C.P. (Lond.). 636 pages, illustrated $11.50. St. Louis: The C.V. Mosby Co. 1953.

[2] BLOCKADE UND CHIRURGIE DES SYMPATHICUS. By Dr. Felix Mandl. 388 pages, with 63 illustrations. $12.40. Wien: Springer-Verlag, 1953.

[3] THE BOOK OF HEALTH; A MEDICAL ENCYCLOPEDIA FOR EVERYONE. Compiled and edited by Randolph Lee Clark, Jr., B.S., M.D., M.Sc. (Surg.), and Russell W. Cumley, B.A., M.A., Ph.D. 768 pages, with 1,400 illustrations. 1st ed. $10.00. Houston, New York: Elsevier Press Inc., 1953.

medicine," has no counterpart in medical literature in our language, and the editors deserve great credit for the comprehensive and encyclopedic volume they have produced.

"Understandest thou what thou readest?" asked Philip of the Queen's minister (Acts of the Apostles, VIII, 30) as he rode in his chariot. The same question might possibly occur to the medical man as he reads through the eyes of a layman this well illustrated volume. Many chapters, however, do make interesting and informative reading for the intelligent reader who would learn more about the human body and the ills to which it is subject. Some chapters, for example those on embryology, disease producing organisms, the brain and nervous system, are "tougher" assignments, but they are written for the most part with care to avoid difficult and technical terminology and are so well and so profusely illustrated that the layman cannot help but be interested and enlightened.

Chapters on "Life Begins," an account of the development of the human from fertilization of the ovary to parturition; the child, its growth and development; the body—how it functions as a machine; and disease producing organisms are followed by chapters on the respiratory system, the blood and blood forming organs, the heart and circulation, the skeleton and muscles, the skin, the endocrine system, the brain and nervous system, the teeth, the digestive system, the urinary system, the reproductive system, the breast, the eye and the ear. In each chapter a general plan is followed: anatomic description is followed by a discussion of the physiology of the organs in question, of the changes produced by disease and finally of the symptoms and treatment of the disorders caused by pathologic changes. In addition there are excellent chapters on the mind, on geriatrics, nutrition, on physical injuries and first aid, on tropical diseases, sanitation, medicine and the law, and medical history.

Since practically all of the contributors are teachers of high rank their contributions have the merit both of being prepared by experts in their particular field and of being written by men skilled in presentation.

Every student of medicine and dentistry and of the biologic sciences, and every high school and college teacher of biology and physiology can obtain accurate information and helpful orientation from this volume. The busy and harassed practitioner will find in it both useful summaries in fields of medicine of which his knowledge may be uncertain, and excellent portraits and interesting thumb nail sketches of many of the men ancient, medieval and modern, who have made distinguished contributions to medical science. Medical men in every field can well recommend it to intelligent and inquiring patients.

SUMNER L. KOCH.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

THE PHYSIOPATHOLOGY OF CANCER; A TREATISE FOR INVESTIGATORS, PHYSICIANS, AND STUDENTS. Edited by Freddy Homburger, M.D., and William H. Fishman, Ph.D. With 28 contributors. Foreword by C. C. Little. 1031 pages, 150 illustrations. $18.00. New York: Paul B. Hoeber, Inc., Med. Book Dept. of Harper & Bros., 1953.

LEHRBUCH DER GEBURTSHILFE UND GYNAEKOLOGIE. By E. Anderes, H. Guggisberg, and Th. Koller. Vol. 2. LEHRBUCH DER GEBURTSHILFE. By Prof. Dr. E. Held, Dr. O. Kaeser, Prof. Dr. Th. Koller, Dr. A. Reist, Prof. Dr. H. Schultheiss, Prof. Dr. R. Wenner, Prof. Dr. A. Werthemann, Prof. Dr. H. Willi, and Prof. Dr. G. Wolf-Heidegger. 2nd rev. ed. Basel: S. Karger, 1952.

POLITIA MEDICI; AN ESSAY ON THE PHYSIOLOGY OF SOCIETY. By Jerome Head, M.D. 267 pages. 1953.

L'AGE CRITIQUE. By Paul Guilly. 126 pages. Paris: Presses Universitaires de France, 1953.

REGIONAL BLOCK; A HANDBOOK FOR USE IN THE CLINICAL PRACTICE OF MEDICINE AND SURGERY. By Daniel C. Moore, M.D. 373 pages, 262 illustrations. $11.00. Springfield, Ill.: Charles C Thomas, 1953.

PEDIATRIC GYNECOLOGY; WITH SELECTIONS ON UROLOGY AND PROCTOLOGY. By Goodrich C. Schauffler, M.D. 3rd ed. 318 pages, 76 illustrations. $7.50. Chicago: The Year Book Publishers, Inc., 1953.

PEPTIC ULCER; PAIN PATTERNS, DIAGNOSIS AND MEDICAL TREATMENT. By Lucian A. Smith, M.D., F.A.C.P., and Andrew B. Rivers, M.D., F.A.C.P. Foreword by George B. Eusterman. 576 pages, 208 illustrations. New York: Appleton-Century-Crofts, Inc., 1953.

AN ATLAS OF PELVIC OPERATIONS. By Langdon Parsons, M.D., and Howard Ulfelder, M.D. 231 pages, 197 plates, $18.00. Philadelphia, London: W. B. Saunders Co., 1953.

PERIPHERAL NERVE INJURIES; PRINCIPLES OF DIAGNOSIS. By Webb Haymaker, M.D., and Barnes Woodhall, M.D. 2nd ed. 333 pages, 272 illustrations. $7.00. Philadelphia and London: W. B. Saunders Co., 1953.

MODERN TRENDS IN DIAGNOSTIC RADIOLOGY. J. W. McLaren, M.A., M.R.C.P., F.F.R., D.M.R.E. 2nd series. 413 pages, 359 illustrations. $18.00. New York: Paul B. Hoeber, Inc., Med. Book Dept. of Harper & Bros., 1953.

THE HYPERTENSIVE DISORDERS OF PREGNANCY. Ernest W. Page, M.D. 120 pages, 2 illustrations. $3.75. Springfield, Illinois: Charles C Thomas, 1953.

THE FUNDAMENTALS OF RADIOGRAPHY. Medical Division, Eastman Kodak Company. 8th ed. 100 pages, 45 illustrations. Rochester, N. Y.: Eastman Kodak Co., 1953.

DISEASES OF WOMEN. By Robert James Crossen, A.B., M.D., F.A.C.S. 10 ed. 935 pages, 990 illustrations. $18.50. St. Louis: The C. V. Mosby Co., 1953.

PREGNANCY WASTAGE. Proceedings of a Conference of the Committee on Human Reproduction, National Research Council, for the National Committee on Maternal Health, Inc. Edited by Earl T. Engle. 254 pages, illustrated. $8.50. Springfield, Ill.: Charles C Thomas, 1953.